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SIMPLE EXCISION IN THE TREATMENT OF PULMONARY TUBERCULOSIS

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THIS preliminary report concerns an experience of a year in the surgical removal of pulmonary tuberculous foci which remain after continuous daily antimicrobial therapy with streptomycin and PAS has been in force for four months or longer. The practice has been to perform local excision of diseased areas, usually with disregard for the segmental anatomy of the lung, and the rationale for this surgical procedure is based on three principles. The first principle relates to the significance of the necrotic (caseous) tuberculous focus as the cause of clinical relapses of the disease. The second principle concerns the absence of tubercle bacilli in sputum, for it is our belief that many of the postoperative tuberculous complications are related to operation performed at a time that the sputum contains organisms. The third principle relates to a conservation of good functioning lung tissue, for in most patients the most dangerous pulmonary disease is located in the superior and posterior portions of lobes of lung.

At this date, thirty patients have been operated upon, and the immediate results have been sufficiently encouraging to warrant a continuation of the program. The patients are in two distinct groups with regard to the extent of the pulmonary disease on admission to the hospital. One group consists of four patients with disease of minimal extent, none of whom had shown tubercle bacilli in repeated cultures of sputum or gastric washings during hospitalization. The logic back of the operative procedure in these cases was based upon

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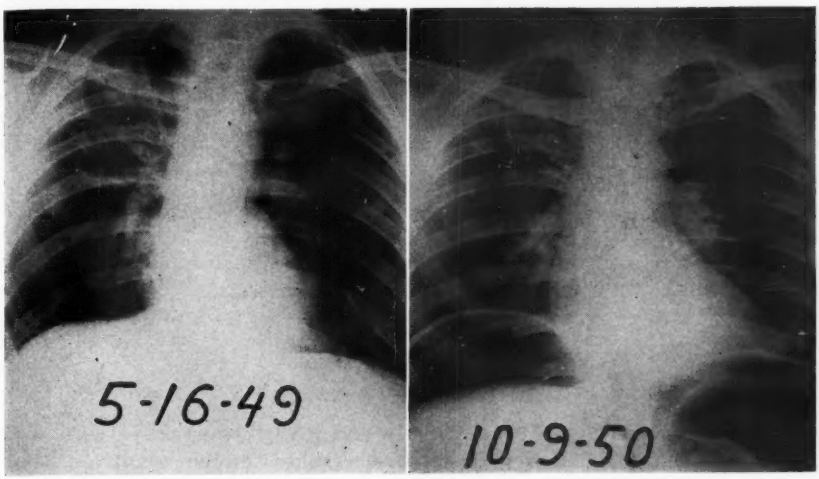
the report of one of us[1] that minimal pulmonary tuberculous disease always contains one or more necrotic lesions; and generally is a localized lesion in the superior and posterior portions of lobes of lung. It should, therefore, be possible to remove the necrotic lesions completely by a small local excision. The remaining twenty-six patients had moderately (sixteen cases) or far-advanced (ten cases) pulmonary disease on admission to hospital. None had had positive cultures of sputum or gastric contents for many weeks or months prior to surgery, although most had shown repeated positive cultures or smears of sputum prior to and early in the course of chemotherapy.

CARDINAL POINTS IN THE PATHOGENESIS OF PULMONARY TUBERCULOSIS

Pulmonary tuberculosis is an infectious disease which is induced by the inhalation of an extremely minute air-borne particle that contains tubercle bacilli. This particle may, by chance, lodge in any portion of the lung parenchyma, and a minute microscopic focus of lobular pneumonia is produced at the site of deposit. Unless this particle lodges in a vulnerable spot in the lung (the upper and posterior portions of pulmonary lobes in the adult[1]), the diseased area seldom becomes more than a few millimeters in diameter and eventually heals without any further dissemination. The common finding of single fibrocalcific nodules in the lower and anterior portions of the pulmonary lobes at necropsy on persons who die from causes other than tuberculosis is ample proof that tuberculous foci in these regions very commonly heal. However, it is common, although not universal, for bacilli-containing particles that lodge in the superior and posterior portions of pulmonary lobes to induce a progressive pulmonary disease. The cardinal difference between the initial disease in these locations is that the necrotic focus in the lesion in the upper portions of lobes commonly sloughs into its connecting bronchus whereas sloughing of lesions in other areas seldom occurs. From this, it is readily seen that the process of necrosis and of sloughing of the necrotic lesion into the bronchial tree is a most important element in progressive pulmonary tuberculosis.

The complex morphologic picture that occurs as a result of the dissemination of the disease through the bronchial tree has been presented previously by one of us,[2] and at present only two phenomena will be mentioned. Frequently there are considerable areas of pneumonia which do not procede to necrosis. These areas of disease are reversible, and heal either by complete resolution or by scar formation. Other areas undergo necrosis and are irreversible. These form the well-known necrotic pneumonic lesion (the caseous lesion) which essentially is a tuberculous abscess. These abscesses may soften up and slough into the connecting bronchus early or they may remain with the dead framework of the lung intact within the necrotic zone for many months, or even years. All of the necrotic pneumonic areas have a tendency to slough and the larger the lesion the greater is the hazard because an organization by fibrosis is extremely slow and difficult. A discharge of the softened necrotic debris into bronchi leads to the formation of the tuberculous cavity and, since the necrotic area is seldom cleanly sloughed, the cavity "wall" is composed to a



A. *B.*

Fig. 1*A*.—A 32-year-old, white man who had acute onset of pulmonary tuberculosis in February, 1949, with progression on strict bed rest. There is a large cavity with a fluid level in the apex of the RLL, pneumonic infiltrate and multiple cavities in the RUL, and an infiltrate in the left midlung field.

Fig. 1*B*.—This is the same patient after seventeen months of continuous daily streptomycin and PAS. The pneumonic component has resolved. The cavities are filled in, leaving solid lesions.

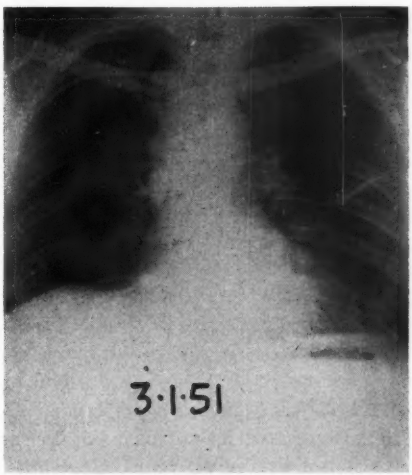


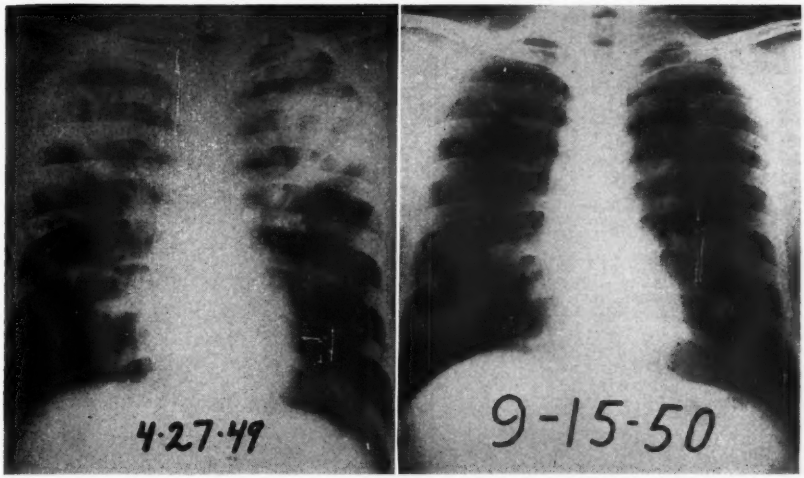
Fig. 1*C*.—Bilateral resection has been completed. Three segments and two wedges were removed from the right lung. A single wedge was removed from the lingula. He has had fourteen negative postoperative sputum cultures. M. B. C. preoperative 128 l/min, postoperative 132 l/min.

greater or lesser extent of necrotic lung tissue. It is this situation that makes a complete healing of cavity by scar formation so difficult and that leaves on "closure" of cavity an area of necrotic material surrounded by scar tissue with the patent connecting bronchus remaining or only plugged by inspissated debris. Such a filled-in cavity can again become an open cavity if the inspissated contents become sufficiently fluid to flow down the bronchus. It is the common persistence of the unhealed necrotic pneumonic tuberculous lesions in persons who have become clinically well of the disease that are the cause of relapses of the disease at a later date. These necrotic lesions usually harbor living bacilli for a long time and, although the numbers of bacilli are extremely variable, they sometimes are present in tremendous numbers even if they are not demonstrable in sputum. Unless these necrotic lesions are eradicated by one means or other, they constitute a major threat to the continued health of the tuberculous patient.

ANTIMICROBIAL THERAPY

The effect of combined streptomycin and PAS therapy in patients with moderately or far-advanced pulmonary tuberculosis at Sunmount are being reported by D'Esopo and Raleigh.[3] The emergence of a bacillary population that is resistant to either chemical agent is greatly delayed, and the degree of resistance that develops is of a lesser order than if either agent is used alone. Clinical relapse even under continuous treatment for two years has been rare, and over 80 per cent of the patients have had their sputum become and stay negative for bacilli. A gradual and progressive clearing of pulmonary roentgenographic shadows takes place over a period of months to a point beyond which stable roentgenographic shadows remain. Tuberculous cavity-formations usually are lost to view with shadows of demonstrable size remaining. These roentgenographic changes, interpreted on a pathologic basis, are considered to represent a disappearance of the reversible pneumonic areas, a persistence of the necrotic pneumonic lesions and a filling in of cavities. These observations apply to patients who previously had not been treated chemotherapeutically. The results obtained in the retreatment of patients is much less satisfactory.

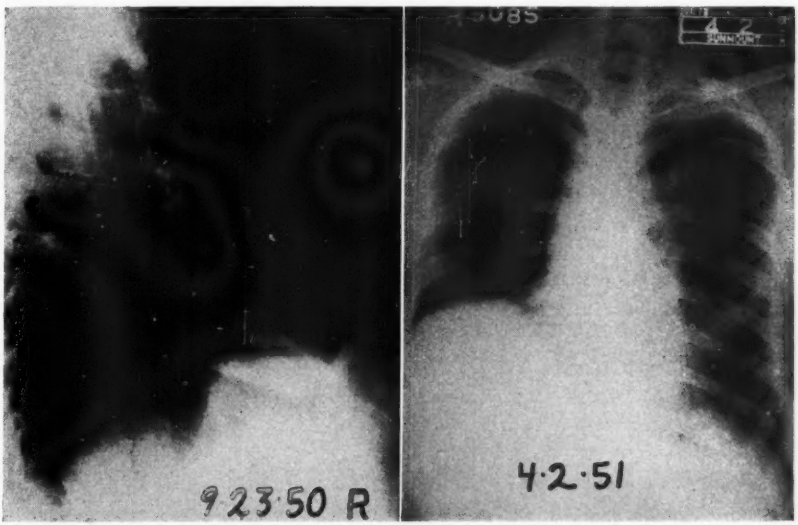
In this series, the effect of long-term streptomycin and PAS on minimal lesions has been observed both from a clinical and pathologic point of view. In the past, dissatisfaction has often arisen with the treatment of small lesions in young medical students, doctors, and nurses who have broken down during training and are so commonly sent to one of the sanitoria in the Saranac Lake area for treatment. Most of these young people have recovered permanently after a reasonable course of bed rest. However, a fair proportion of them have had second, third, or fourth breakdowns shortly after they were allowed to resume activity and, in spite of a variety of forms of treatment, have continued to be patients over a period of five or six years. It would seem logical that by doing small resections on these early localized lesions, one might eliminate, then and there, the dangerous portion of the infection and prevent these spreads and prolonged periods of invalidism. Residual necrotic foci have been



A. *B.*

Fig. 2*A*.—A 31-year-old white man who had an acute onset of pulmonary tuberculosis in February, 1949, with high fever, toxemia, and acute tuberculous laryngitis. There is a large cavity in the apical segment of the right lower lobe, a pneumonic infiltrate, and multiple cavities in both upper lobes. Streptomycin and PAS were begun at this time.

Fig. 2*B*.—This is the same patient after seventeen months of continuous daily streptomycin and PAS. Only dense shadows remain, representing necrotic foci and filled-in cavities. The pneumonic component has disappeared.



C. *D.*

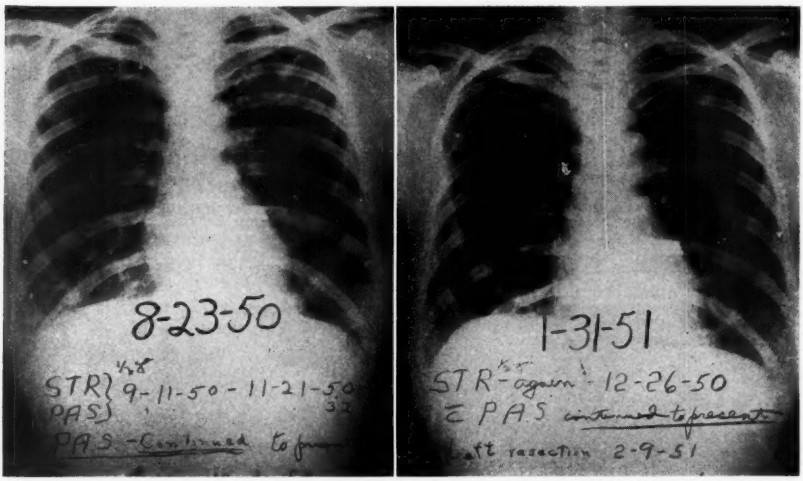
Fig. 2*C*.—The right lateral view shows the filled-in cavity in the apical segment of the right lower lobe and the dense shadows in the posterior segment of the right upper lobe where there previously were multiple cavities.

Fig. 2*D*.—Bilateral resection has been completed. Three segments and one wedge were removed on the right. On the left, three large wedges were removed. The right phrenic was inadvertently divided at operation. He has had ten negative sputum cultures postoperatively.

found in each patient operated upon for a minimal lesion, and tubercle bacilli have been shown to be present in each lesion despite repeated negative gastric and sputum cultures.

SURGICAL APPROACH

Surgical intervention is timed to the individual patient. Disappearance of bacilli in sputum and the establishment of stationary roentgenographic picture is awaited. Advancement of the date of operation is unnecessary in the fear that resistant organisms may emerge in large numbers or that the benefit of chemotherapy may be lost before surgery is instituted. To locate and evaluate lesions prior to surgery, serial roentgenograms, lateral and oblique views, and planigrams are studied.



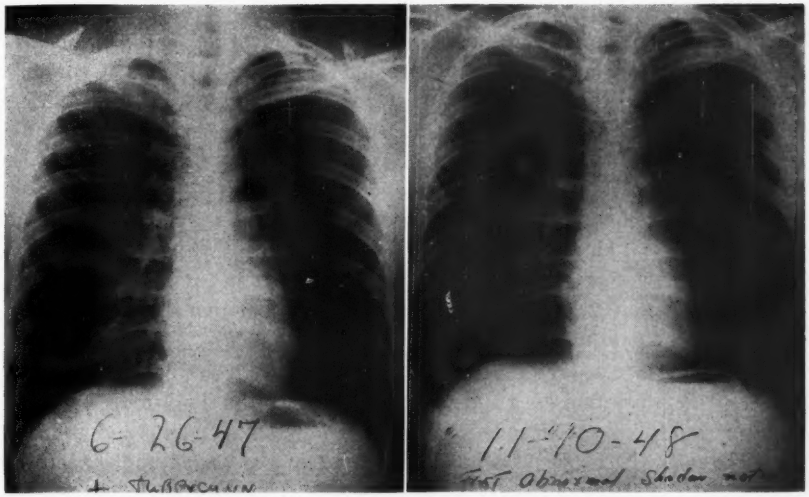
A. *B.*

Fig 3*A*.—This is a 40-year-old nurse who contracted minimal tuberculosis in 1938. She has had four breakdowns in thirteen years and has gradually become worse. She has cavitary disease on the left side.

Fig. 3*B*.—This is following wedge resection on the right side. This is the only patient in the series in which the streptomycin course was interrupted. Wedge resection was performed on the left upper lobe on Feb. 9, 1951.

At exploration, the entire lung is carefully palpated to determine the amount of excision that is necessary. The necrotic lesions are easily detected, even if they are only a couple of millimeters in diameter. Usually filled-in cavities are easily palpated, although these may not be as firm to the touch as unsloughed necrotic foci. Commonly the lung feels normal in large areas which previously had shown extensive roentgenographic shadows. Little difficulty has been encountered in locating lesions which were indicated by roentgenographic shadows; however, it has not been unusual to find significant lesions which were not suspected from study of roentgenograms.

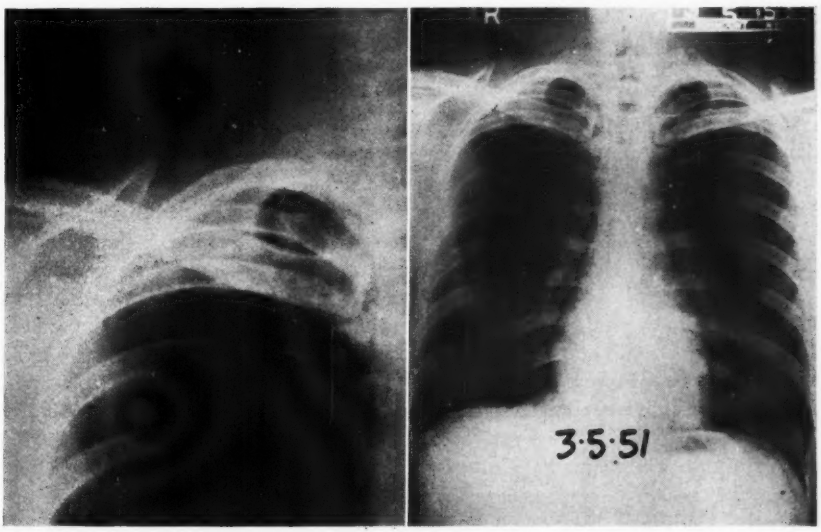
The amount of lung tissue to be excised is determined after a complete palpation of the lung has been made with the preservation of a maximum



A. *B.*

Fig. 4*A*.—This is a 27-year-old physician whose tuberculin became positive at this time. It had been negative less than a year previously. No abnormal shadow was seen in the roentgenogram.

Fig. 4*B*.—An abnormal shadow was first noted at the right apex at this time.



C. *D.*

Fig. 4*C*.—This is a magnification of the previous film showing the lesion at the right apex.

Fig. 4*D*.—A wedge of necrotic tuberculosis (minimal lesion) was removed from the apex of the right upper lobe. The patient received four months of streptomycin and PAS preoperatively, and four months of both drugs postoperatively. Since Jan. 1, 1952, he has been working full time as a resident physician.

amount of functional lung being carefully considered. Usually only wedges of lung are resected, although on occasion the removal of an entire lobe or a lung may be necessary. Some patients have many small nodules scattered throughout a lobe or a lung and, in such instance, one hesitates to sacrifice so much healthy lung parenchyma. The nodules located in the superior portions of lobes are resected, usually by wedge resection, because they are located in the vulnerable portions of lobes.[1] Wedges may be removed from other parts of the lung if numerous nodules are present in the area. In any location, lesions over 0.5 cm. have been removed singly. As many as nine wedges have been removed from the same patient. Minute lesions in the lower portions of lobes are left undisturbed on the pathologic basis that there is a strong tendency for small necrotic lesions in such locations to heal.

The surgical technique in itself is simple. The wedge to be resected is outlined, the pleura is incised a short distance beyond the disease area, and the ara is excised en bloc. Sutures are applied to bleeding points and bronchial leaks. Usually the large bronchus at the apex of the wedge has appeared to be normal and is easily ligated. In most instances, no effort has been made to pleuralize the raw surface or to close the defect by approximating the edges. However, in a few instances, persistent small bronchial leaks have been controlled either by placing gelfoam or pleural grafts on the raw surface. Not infrequently, the disease may appear too deeply located to allow a wedge resection. However, experience has shown that after the segmental vessels and bronchi have been dissected out, the diseased area can be lifted away from the hilum, and a wedge or subsegmental resection can be performed.

EARLY RESULTS

Prior to Feb. 1, 1951, thirty consecutive wedge or subsegmental resections have been done with bilateral resections in three patients. The pathology in each resected specimen showed necrotic pneumonic lesions and the cavity-bearing areas removed showed filled-in cavities with patent bronchial communications. Otherwise there were areas of scarred tissue with extremely little evidence of unhealed nonnecrotic pneumonic lesions. The bronchi at the resected end of the wedge have showed little evidence of disease other than some lymphocytic infiltration of an intact mucosa. Tubercle bacilli have been demonstrated in one or more necrotic lesions in every case, although not in all lesions. Patent bronchial communications with some necrotic lesions were demonstrated microscopically, although they were not found macroscopically. Two hundred three postoperative cultures of sputum or fasting gastric contents for tubercle bacilli have all given negative results. There has been little change in the cardiorespiratory reserves postoperatively, as compared to preoperative findings. Nearly all have had preoperative and postoperative pulmonary function studies. No postoperative tuberculous complications have arisen. No complications of any sort have occurred in the four patients with minimal disease. As a rule, the postoperative course has been benign. At present, all patients are in excellent physical condition. The following is a list

of complications that have been encountered and that one might expect to occur following the surgical procedure used:

Number of Operations		30
Hemothorax requiring postoperative evacuation	1	
"Atelectasis" requiring bronchoscopic evacuation	1	
Division of phrenic nerve (inadvertent)	1	
Wound infection	0	
Empyema	0	
Bronchopleural fistula	0	
Increase of pulmonary tuberculosis	0	
Total	3	(10%)

CONCLUSION

It is fully recognized that these early results give only a part of the picture, and that a lapse of five years may be necessary for the story to be completed. It is not claimed that this approach to the surgical problem of the tuberculous lung will eradicate all of the pulmonary disease; however, it is anticipated that the small lesions left behind will cause no further trouble. There is maximum conservation of normal functioning pulmonary parenchyma. However, if this approach to the problem does not yield results superior to other accepted methods of treatment, then it can be definitely concluded that pulmonary tuberculosis is not a disease that can be controlled by surgical excision.

ADDENDUM

Feb. 18, 1952. Follow-up to date reveals no clinical or roentgenologic relapse in this series. One patient has had two positive sputum cultures since operation. He had received previous courses of streptomycin.

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2. Medlar, E. M.: Pathogenetic Concepts of Tuberculosis, Am. J. Med. 9: 611, 1950.
3. D'Esopo, N. D., and Raleigh, J. W.: Am. Rev. Tuberc. in press.

When this paper was presented at Atlantic City the section in the text on Pathology was omitted due to time limitation. The following discussion by Dr. Welles was put in to clarify the pathologic concepts on which the surgery was based.

The slides referred to in Dr. Welles' discussion are color plate Illustrations I and II.

DISCUSSION

DR. EDWARD S. WELLES, Saranac Lake, N. Y.—I am sorry Dr. Medlar is not here to discuss the pathogenesis and the pathology of tuberculosis. Most of us probably feel that we understand the pathology of tuberculosis thoroughly, but I have had to change my way of thinking about it since associating with Dr. Medlar, and possibly I can explain his thoughts to you.

We have been taught in the past that the process is the invasion of the lung by tubercle bacilli, followed by acute inflammatory reaction with invasion polys which are later replaced by lymphocytes and giant cells; caseation can occur in the center of a lesion and then be replaced by the infiltration of fibroblasts and formation of a scar. The trouble with thinking about tuberculosis in that way is that that happens in microscopic lesions and the demonstration of that process which has been shown so well by many pathologists and which was taught for years by Dr. Leroy Gardner, is that the demonstration was made with a microscope. All that picture can be shown in the microscope. But Dr. Medlar has shown

The following illustrations are from tuberculous lung tissues which were surgically removed. They were selected to portray the different phases in the pathology of pulmonary tuberculosis. Illustrations V and VI were from the lesions shown in roentgenograms Figs. 3*A* and 3*B*. Illustration VII is from the lesion represented in roentgenograms Figs. 4*A*, 4*B*, 4*C*, and 4*D*. Roentgenograms from the other illustrations are not shown.

Illustrations I, II, V, and VI are enlarged five diameters, III and VII are enlarged seven diameters, IV is enlarged thirty diameters, and VIII is enlarged fifteen diameters.

Illustration I.—This illustrates an area of "nonnecrotic" tuberculous pneumonia that is composed of "epithelioid" tubercles and of areas of lobular pneumonia without evidence of necrosis, other than microscopic areas, either of the lung framework or the inflammatory cellular reaction. This is the "reversible" phase of the pathology of pulmonary tuberculosis and represents the disease which "clears" roentgenographically during "bed rest," pneumothorax, or proper chemotherapy.

Illustration II.—This illustration shows a "necrotic" or "caseous" tuberculous pneumonia of about the same size as in Illustration I. This is the "irreversible" phase of tuberculous pneumonia. This phase of the disease remains after "bed rest," pneumothorax, and chemotherapy, and constitutes the hazard of "relapse" of the disease after "clinical" recovery. It is this type of lesion which gives rise to cavity formation if it softens up and sloughs through the bronchus which connects with the necrotic area. In this particular lesion no bacilli were found however in many lesions which are morphologically identical bacilli are often present in large numbers. This lesion is an endobronchial dissemination or metastasis and was present in the lower posterior portion of an upper lobe.

Illustration III.—This illustration is from the apical area of the same lobe as the lesion in Illustration II. There are five small "necrotic" pneumonic lesions present. One of these small lesions showed large numbers of bacilli. Since the superior portions of pulmonary lobes are the most vulnerable portions of the lung in tuberculosis, lesions of any size in these regions should be excised when palpated on exploration of a lung. Both size and location of lesions need to be considered in the decision of excision.

Illustration IV.—This old necrotic lesion was removed from a patient who had been known to have pulmonary tuberculosis for eight years, and who had had four separate hospital admissions. Before surgery the patient had been on continuous combined streptomycin and PAS for over a year. The lesion illustrated measured only three millimeters in diameter and was not visualized in roentgenograms, but was easily palpated at operation. This represents one of the small local excisions commonly made. Note the bronchus connecting directly with the necrotic area and having necrotic debris within its lumen. The bronchial lining epithelium is normal up to the point at which it abuts upon the necrotc area. A peripheral zone of well-formed fibrotic tissue surrounds the necrotic area except at the point of bronchial connection. This is a common situation and is the principal factor which allows pulmonary tuberculosis to be an unpredictable disease that has a strong tendency to relapse. Bronchi commonly are plugged by necrotic debris but rarely are obliterated by scar formation across their lumen.

Illustrations V and VI.—These two illustrations are from the two lungs of the same patient. Illustration V shows the pathology found in a "wedge" resection after combined streptomycin and PAS had been in effect for one month. Both "nonnecrotic" and "necrotic" areas of tuberculous pneumonia are present. Illustration VI shows the pathology present in a "wedge" resection from the opposite lung after combined streptomycin and PAS therapy had been in effect for six months. During this time considerable "clearing" of roentgenographic shadows had occurred in the area from which the "wedge" was removed. In this section only "necrotic" lesions and some scar formations are present. The lesion represented in Illustration V had shown a stationary roentgenographic shadow for five years. Tubercle bacilli were demonstrated in necrotic lesions on both sides, both in tissue section and by culture. Although this patient had had four relapses over a period of twelve years, tubercle bacilli had never been demonstrated in the sputum.

Illustration VII.—This illustration is a cross-section of a small wedge of lung tissue removed from a patient with "minimal" pulmonary tuberculosis. The patient first reacted to tuberculin in 1947, and showed a small shadow in the area resected in 1948. The shadow persisted after one year of "bed rest" therapy and an additional four months of combined streptomycin and PAS therapy. The wedge of lung removed measured about 2.5 cm. across. Serial section of the entire specimen showed the presence of six separate lesions—two of which were largely scar tissue and the other four were similar to the lesions in the illustration. In one of the scarred areas was an organizing old necrotic focus which was interpreted as the initial necrotic lesion from which the others were disseminated. The three lesions in the illustration show a peripheral organizing zone of granulation tissue and a central "core" composed in large part of neutrophiles. Tubercle bacilli in small numbers were found in the exudate in these lesions but were not found in the scarred areas. Only an occasional epithelioid tubercle and giant cell was found in the serial sections.

Illustration VIII.—This illustration is from a small wedge of lung tissue removed from a patient with a history similar to that of the patient illustrated in Illustration VII, with the exception that the date of conversion to a reactor to tuberculin was not known. Also this patient showed an increase of disease near the end of his course of bed-rest therapy. He was then started on combined streptomycin and PAS therapy and after five months of this treatment the roentgenographic shadows had receded to their original size. The specimen removed contained two fibronecrotic foci which measured about three millimeters across and a larger lesion which measured six tenths by one centimeter. The largest lesion was serial sectioned and the illustration from one level of the serial sections. This lesion proved to be a minute cavity formation partly filled with necrotic material and it also had a patent bronchial communication. An occasional tubercle bacillus was found in the necrotic contents of the cavity. At one side of the larger lesion is seen a fibronecrotic focus which measured less than two millimeters across and which had a small calcific center. At another level this old focus becomes an integral part of the larger lesion and it seems probable that this was the source from which the larger lesion had its origin. This clearly portrays the complexity frequently encountered even in small and seemingly insignificant tuberculous lesions.

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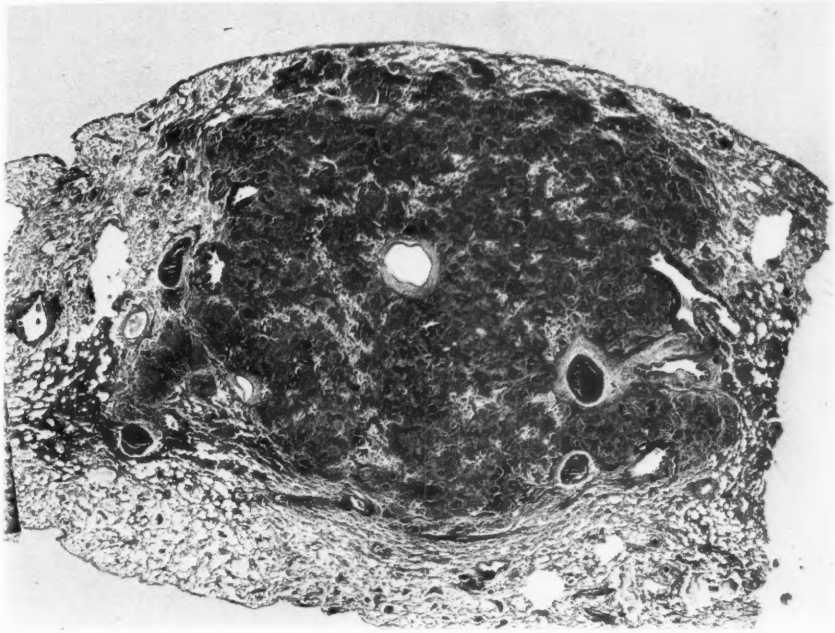

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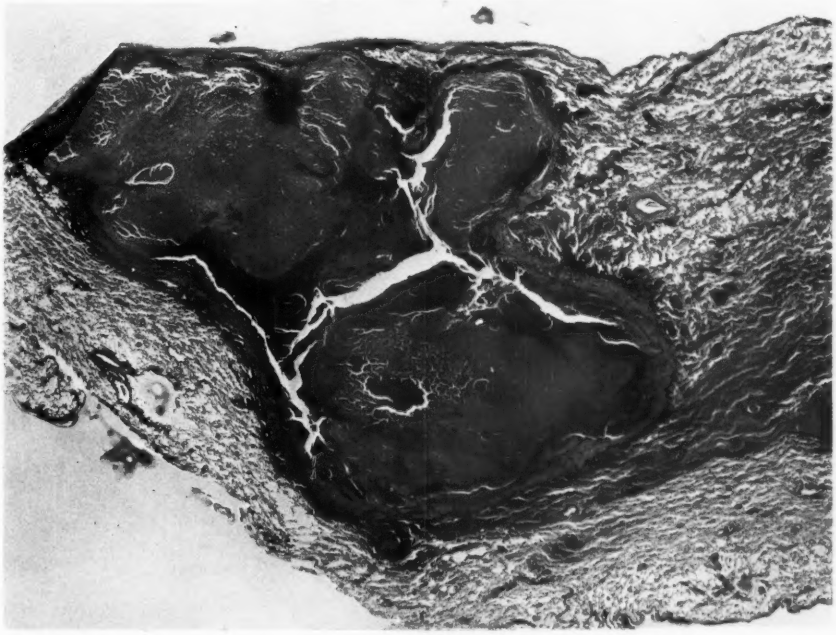

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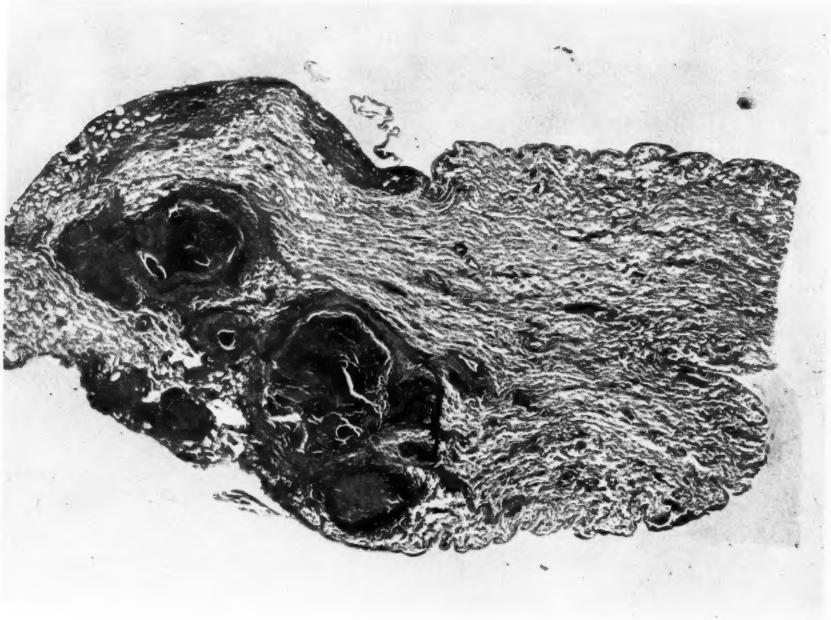

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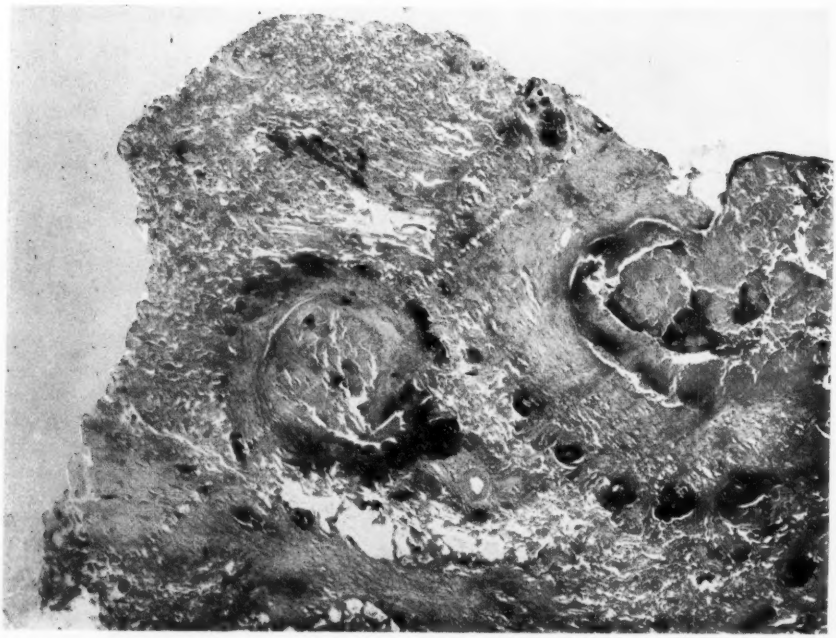

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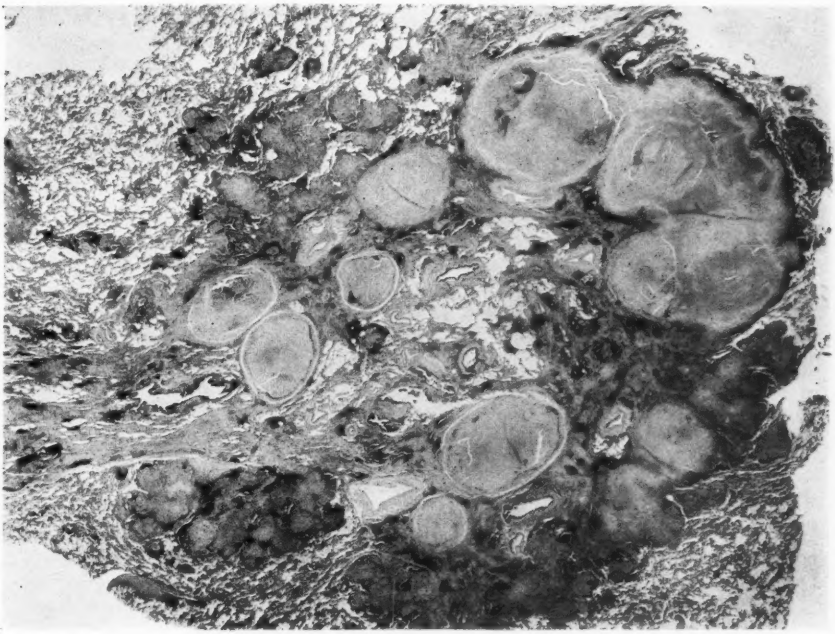

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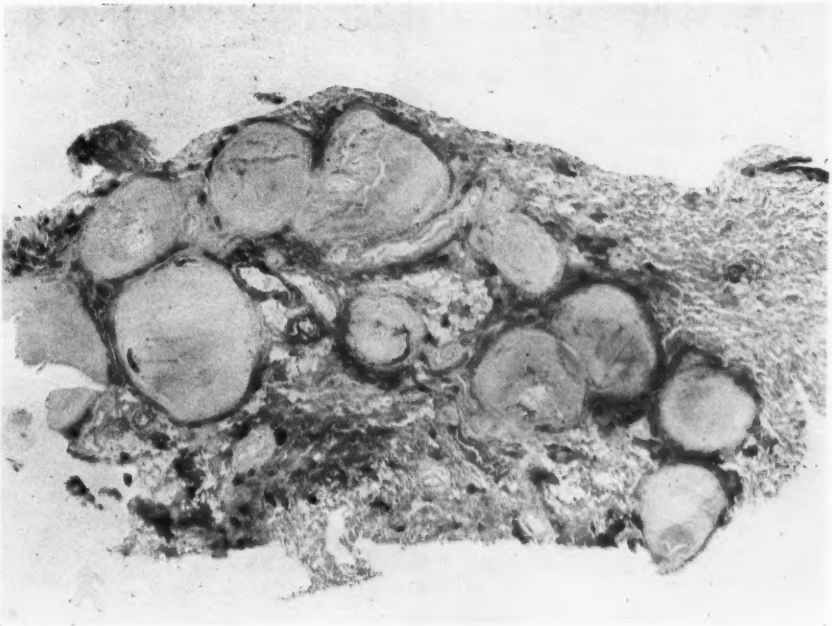

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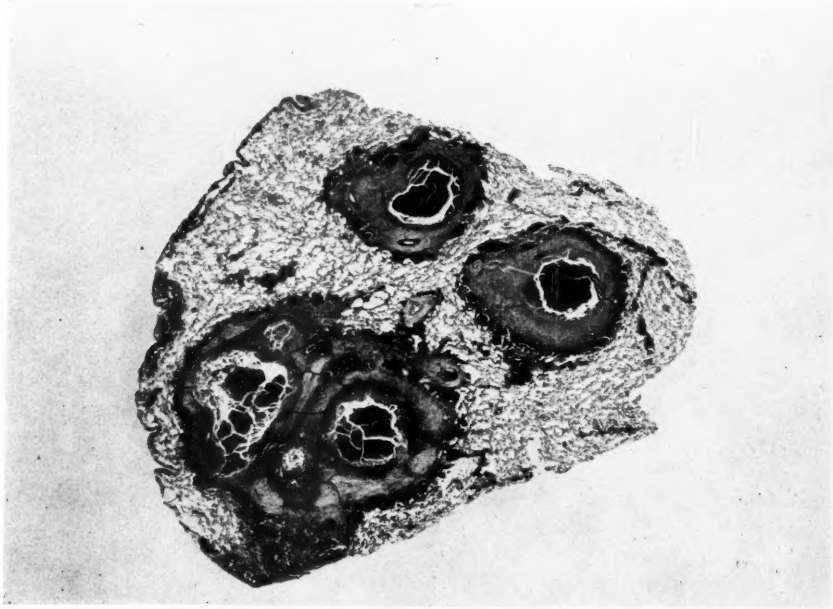

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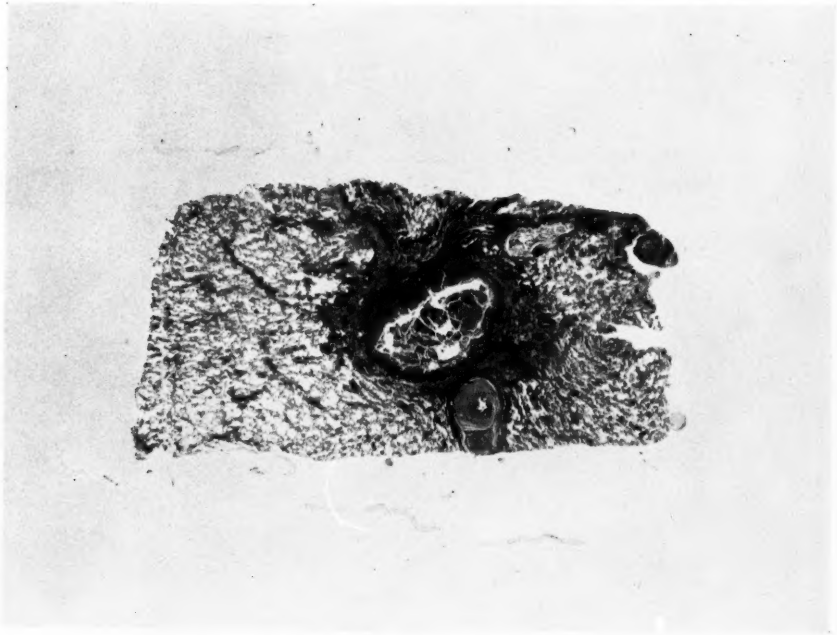

VIII.

over the years that there are definitely two types of tuberculous processes in the lung. If a lobule of the lung is invaded by a relatively small number of tubercle bacilli, and their virulence is not too high, tuberculous pneumonia occurs. If another lobule is invaded by an overwhelming number of bacilli, or very virulent bacilli, the tissue is killed and necrosis occurs, and these necrotic areas can be of almost any size.

(Slide.) (Color plate I.) This is the typical lobule full of tuberculous pneumonia. There is no destruction of tissue except in small microscopic areas. You will get a better idea of the lesions Dr. Ryan showed if I tell you the size of these. None of the colored slides shown by Dr. Ryan, and neither of these, is a magnified microphotograph; they are sections. This is an actual section of the lung, and the size is about one centimeter vertically by two centimeters horizontally. This is a reversible lesion. Under rest treatment this lesion can go on and heal and leave practically normal lung. Under antibiotic treatment it will heal and disappear and leave a clear shardow in the roentgenogram. At the present time this lesion leaves a solid shadow in the film which is indistinguishable from the lesion shown in the next slide.

(Slide.) (Color plate II.) This is almost identically the same size lesion, about one centimeter by two centimeters—as large as the joint of my thumb. There is no magnification here except what is given by the projector. This is a necrotic, destroyed area that cannot return to normal under rest treatment, under pneumothorax, under antibiotic treatment. Fibroblasts cannot work into this lesion from the capsule, replace the necrotic caseous material, and turn this lesion into a scar. I have had arguments with pathologists—"We have seen this fibrosis take place in necrotic lesions." I remind them that they have seen that happen under the microscope, but have not seen it happen in lesions as big as the end of my finger like this one. The only way this lesion can disappear is by liquefying, emptying out, through its bronchus, which is there and open. That can happen without spread of tuberculosis if the material is all coughed up; or it can produce spread as it is liquefied. If it liquefies, empties out, becomes then a thin-walled cavity, the walls can fall together and it can become a scar.

These are the lesions left after long-term antibiotic therapy. These are the ones we are removing and these are the ones we are finding in minimal disease and taking out, hoping that we will prevent recurrence over and over again in these young people.

(Slide.) This is a diagram that Dr. Ryan drew to show that the connection of the bronchus to the necrotic lesion is present, but the finding of it and showing it in the section is a matter of luck. We have often been told by the pathologists that a lesion is completely encapsulated. If the section is cut where the vertical line is you will find, as you saw in many of Dr. Ryan's sections, a completely round encapsulated lesion with a rather thin capsule all the way around it. Obviously it has no bronchial connection. Obviously it is safe. However, if the section of the same lesion is made in the direction of the slanting line or horizontally at the level of the bronchus, the bronchial connection is immediately apparent. As Dr. Ryan said, bronchial connections, by careful examination by the pathologist, have been demonstrated in practically all these lesions when he took the trouble to look for them.

I simply hope this will give a better picture of our conception of the pathology, when the criticism and discussion start.

DR. JEROME HEAD, Chicago.—During the past few weeks, in my spare time, I have been reading Oswald Spengler's *Decline of the West*. He gives as an inclination of declining civilization the development of virtuosity without a solid basis in reality. I mention this because I feel that as clinicians and surgeons there is a danger that we are giving way to such virtuosity; that we are turning our clinical functions over to the pathologist and bacteriologist. If the bacteriologist by the most delicate methods can culture a single tubercle bacillus from a patient's gastric washings, we are argued into believing that the patient is ill and in need of the excision of something—perhaps a segment of his lung, perhaps a whole lung. We must ask ourselves seriously if the patient with an occasional positive culture on gastric wash following thoracoplasty is a menace to his associates or a menace to himself. Is such a finding an indication for pneumonectomy? I do not believe so.

Similarly, is a patient on whom the pathologist can demonstrate a walled-off focus of tuberculosis or a minimal tuberculous infiltrate which has not healed entirely in the center, clinically tuberculous or clinically threatened? I do not believe so. I believe that we must insist on our rights as clinicians and that in these matters we must refer to experience and statistics.

At Edward Sanatorium, 98 per cent of the patients who entered with minimal tuberculosis were well five to ten years after their treatment with bed rest or pneumothorax. Our results on all the patients who are discharged as arrested show that 85 per cent are well from five to ten years after their discharge. In other words, our over-all recurrence rate is between 10 and 15 per cent. In view of these statistics, I do not feel that we must surgically eradicate every shadow that appears on the roentgenogram. What Dr. Medlar has shown and what Dr. Ryan and Dr. Welles are pointing out, is that we arrest tuberculosis, we do not cure it. After all, what we are after is people who, after treatment, are clinically well and who remain clinically well. I am not at all interested in people who are bacteriologically pure or pathologically beyond criticism.

In saying this I do not mean that this paper is not worth while. It is probable that we will find that certain very large infiltrates are so dangerous as to warrant their resection. But to proceed from this to argue that every infiltrate should be removed is, in my opinion, a tendency toward virtuosity.

DR. ROBERT G. BLOCH, Chicago.—To follow up Dr. Head's remarks, I take the *Decline of the West* for granted but not the decline of tuberculosis. One of the reasons for this is the very type of lesion which Dr. Ryan and Dr. Welles discussed. The so-called early reinfection lesion in a majority of cases proves to be pathologically further advanced than is frequently thought. Any sharply circumscribed shadow of moderate or little density, if it is proved to be tuberculous, can be assumed to be a caseous focus. As such, it is a potential cavity or, in fact, it is a cavity which as yet has not found communication with the bronchial system or where that communication is temporarily blocked. These early reinfection caseous tuberculomas remain the residual problem in tuberculosis, although as time goes by most or all of the involvement emanating from them through the years may heal satisfactorily. It is this residual tuberculoma and potential cavity which poses the essential problem. It is justified to make it one of the aims of surgical attention as the authors have done, but I agree with Dr. Head that it should not be necessary to excise all these lesions. Enough circumferential fibrosis can occur to render them clinically innocuous. If the central caseation is small enough, calcification may eventually occur to result in pathologic healing.

This discussion involves the question of what we should call active tuberculosis. Active tuberculosis is generally conceived as an involvement which is undergoing changes in either direction. This would imply that lesions which fail to do so over a period of time should be called arrested. I believe this is a fallacy and dangerous; any of these so-called arrested lesions which contain caseous material, the breeding place of organisms, is so highly potentially active that to term it as arrested and to send the patient back into active life with that classification is likely to lead to misunderstandings about the further possibilities of the course of the disease. Lesions, therefore, which assumedly are caseous tuberculomas, should be classified as "potentially active." On the other hand, the sound caution, which is always indicated in judging tuberculosis as healed, has induced the authors of the newly republished *Diagnostic Standards and Classification of Tuberculosis* to omit the terms "healed" or "cured" entirely. According to this classification, therefore, the disease is not curable. I should like to go on record as objecting strenuously to that concept, which I believe to have originated largely from the very region from which the authors of this paper hail. We must steer clear of the dangers of overclassification, and provide leeway for a variety of interpretations based on the merits of each individual case. Let us avoid standardization in all aspects of medicine. One of the discussors of

the first paper this morning demanded standardization of surgical technique in tuberculosis. It was one of the most horrible words I ever heard at a medical meeting. Once we reach the point where we want standardized concepts and technique, we will have reached the end of progress.

DR. FRANK B. BERRY, New York.—I think anyone who has followed this work of Dr. Medlar, Dr. Welles and Dr. Ryan carefully, and who has seen their results and talked with them, cannot but be convinced of its soundness and correctness. The lesions you saw on the films and later the sections as shown you by Dr. Ryan, were the residua. They were demonstrable residua of caseous foci, and we all know that caseous foci break down and are a danger; they liquefy and discharge through a bronchus as Dr. Bloch has just told you. The physician whose small apical lesion you saw has come under discussion before, at meetings which I have attended. But I am sure that if it were your lesion and you knew it had not changed for more than a year, and you were walking around with a caseous focus, I am sure you would feel better without it than still carrying it with you.

DR. WARRINER WOODRUFF, Saranac Lake, N. Y.—I am on my feet because I have been following this work closely and, to my mind, this is one of the most important papers dealing with tuberculosis to which I have had the privilege of listening in this Association. I think it represents a fundamental change in concept. Many of the papers we have presented and listened to have been primarily papers on technique. There is still a place for that. Obviously, technique is a very important part of this work. When the authors can present twenty-five consecutive cases of excisional surgery in pulmonary tuberculosis, with no mortality and this low morbidity, that is excellent technique; but I think far more important than that is the change in thinking. In the past our goal has been to arrest the disease and enable the patient to live with it. Dr. Pannier, in his discussion this morning, told of the number of late thoracoplasty deaths from tuberculosis. Any of you in sanatorium work know that, in any series of admissions in any sanatorium, a considerable number are repeaters. The young doctor whom they were discussing this morning—I do not know his identity—is an example, but we have all seen patients who, at one time in the course of their disease, have had a lesion no larger than his. Many permanently arrest their disease, but others we have watched break a second, a third, or a fourth time.

If it is possible to excise the tuberculosis (I realize you cannot get rid of all the bacilli) allowing the body defenses to take over from that point; if, over a period of years it can be shown that the relapse rate is far less than by our present method of treatment; then I think this is going to be a very valuable contribution. When this work was started, I was just as skeptical as Dr. Welles about what could be accomplished. We have listened to Dr. Medlar, we have seen the sections, we have seen the results; and I think most of us who have been following it for some time can be classified as converts. It remains to be seen whether subsequent events will justify our optimism.

There is just one other thing I should like to point out—and I think most of us have been struck by it—namely, the conservation of pulmonary function in Dr. Ryan's cases. One of those he presented had a preoperative maximum minute ventilation of 190 liters and, after multiple resections on both sides, this patient still had 172 liters. That is extremely high. He presented several others with similar findings, but not as high as this one.

These findings are in contrast to the loss of function following thoracoplasty, particularly bilateral thoracoplasty when loss is likely to be extreme. Even in resection I am sure we have all sacrificed too much functioning lung tissue. Several years ago I performed a pneumonectomy for tuberculosis, and in retrospect I am sure that was too much, and even a lobectomy would have been too much. It is entirely possible that a segmental, or even a subsegmental or wedge, would have been sufficient; yet I have seen this same mistake made elsewhere. I am sure many of us in the past have erred by sacrificing far more lung than necessary, both by collapse and by excision.

In summary, this work holds great promise, and if the late results are comparable to the early results, it may revolutionize our thinking on the treatment of tuberculosis.

DR. EDWARD J. O'BRIEN, Detroit.—I am very much impressed with this paper and, as a matter of fact, I am somewhat of a convert myself since listening to it. What impressed me was the fact that antibiotics and collapse have been used for a considerable period before resection. The tendency, in many clinics, is to resect every lesion as soon as it is seen, although a lot of them, we know, do get well and stay well with antibiotics and collapse; but if, after a course of treatment, lesions are standing still or getting worse, I think they should be resected. So-called repeaters should also be resected. One of my greatest hopes is that I may live ten years so that I may see some of this chaos cleared up. Right now it is difficult to get a patient out of a hospital or sanatorium without resection of some sort. The medical men have become very bloodthirsty. You have to be quick on your feet to get a patient discharged with his lungs intact. We, and others, have had a large number of patients get well in the past with only collapse measures, and I am sure will again in the future, but there is such a wide divergence of opinion at present that the situation is chaotic. Opinions vary from resecting every lesion as soon as it is seen, to collapsing a whole lung, and adding paraffin and other packs. If a small caseous center is always going to be such a menace, it is difficult for me to understand how an extensive lesion, that has been collapsed by thoracoplasty, etc., can become healed so frequently, and the patient remain well. We shall have to find a middle ground somewhere, and I think we shall. Medlar's contribution is one of the finest I have heard before this Association, and I think we should take it very seriously. However, I do not believe we shall become as radical as many of the medical men are at the present time, and take out every lesion as soon as we see it.

DR. LEO ELOESSER, San Francisco.—May I ask Dr. Ryan whether his patients, at the end of these resections, turned tuberculin-negative?

DR. RYAN (Closing).—I would like to thank all the discussors. In answer to Dr. Eloesser's question, we have not been testing these patients, but we are certainly going to do so, especially those with minimal lesions; we are going to make tuberculin tests on them in the near future.

With regard to the relapse rate in minimal tuberculosis, our experience is much different from that of Dr. Head. Dr. Roger Mitchell recently studied all the patients discharged from Trudeau Sanatorium in the past seventeen years with minimal tuberculosis. More than 30 per cent of those patients have relapsed.

A STUDY TO DETERMINE THE EFFECT OF PREVENTION OF OVERDISTENTION OF THE REMAINING LUNG TISSUE ON THE ELEVATED RIGHT VENTRICULAR PRESSURES, FOLLOWING THE RESECTION OF LUNG TISSUE IN DOGS

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MANY investigators have worked on the problems of the lung circulation. Tigerstedt[1] gives in his book concerning the physiology of the circulation an extensive report of the many experiments which have been performed since about a century ago. It is generally accepted that the lung contains more blood during inspiration than during expiration, and least when it is overinflated or compressed. The blood flow is the best during inspiration, since the width of the pulmonary capillaries is then larger than during expiration.

Wasson[2] gives a brief review of the more recent literature about this subject, and it is still agreed that the blood flow through the expanded lung is better than through the collapsed one.

Björk and Salén[3] showed in a study that the blood flow through an atelectatic area of the lung is continuously decreasing during the first month, until practically no blood is passing through the nonventilation part of the lungs. At the same time there is no decrease in size of the main branches of the corresponding artery. Therefore, the blood flow is thought to be shut off in the capillary bed, which is gradually closing down.

Removal of lung tissue reduces the size of the pulmonary vascular bed. The right heart, therefore, has to work against a higher resistance. As a result of this there will be a rise in the pressure in the pulmonary artery and the right ventricle. The more reduction of lung tissue, the higher the resistance to the blood flow in the pulmonary vascular bed will be, and the greater the strain on the right heart. All this has been experimentally proved (among others by Carlson and associates[4]).

The resistance in the pulmonary circulation depends on: (1) the number of vessels, and (2) the diameter of the vessels. If marked overdistention of lung tissue would reduce the diameter of the pulmonary vessels, then it would cause an increased resistance in the pulmonary circulation and impose a greater strain on the right heart. Prevention of marked overdistention then should be considered when lung tissue is to be removed.

It was thought that marked overdistention of lung tissue would stretch the capillaries and thus narrow them, so increasing the resistance and the burden on the right ventricle. Prevention of overdistention therefore might

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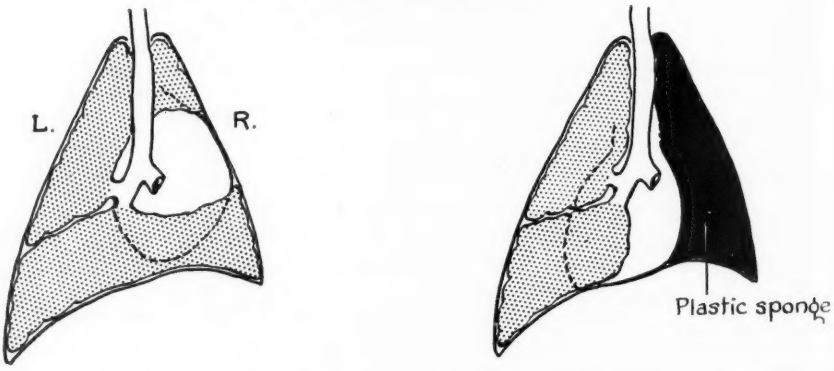
keep the vessels in the more normal shape and might cause less rise in resistance in the pulmonary vascular bed and less strain on the right ventricle.

Following pneumonectomy right ventricular pressures are increased. If overdistention of the remaining lung produces a further increase in right ventricular pressures, one might conclude that there is more resistance and that the width of the pulmonary vascular bed is smaller.

After these preliminary thoughts the following experiment was performed.

TABLE I. RIGHT VENTRICULAR PRESSURES IN MM. HG TWO TO THREE MONTHS AFTER RIGHT PNEUMONECTOMY



LEFT LUNG OVERDISTENDED		LEFT LUNG NOT OVERDISTENDED	
DOG NO.	RIGHT VENTRICULAR PRESSURE (MM. HG)	DOG NO.	RIGHT VENTRICULAR PRESSURE (MM. HG)
36	43/2	821	49/5
379	48/4	795	38/6
394	48/8	815	39/6
436	48/4	602	30/1
437	53/11	612	46/3
486	63/8	362	31/4
		388	25/1
		534	22/2
		64	42/4
		966	38/3
Average pressure	50/6	Average pressure	36/4

TECHNIQUE

Ten healthy mongrel dogs of both sexes, with an average weight of 12 kg., were used. A right pneumonectomy was performed with the dissection technique. To prevent overdistention of the remaining lung, a plastic sponge,* as used by Grindlay,[5] was placed in the right thoracic cavity. Following operation the right ventricular pressure was measured at intervals, and the position of the mediastinum was checked by fluoroscopy. The pressures obtained were compared with those from an earlier experiment in which right pneumonectomies were performed on dogs, the remaining lung becoming overdistended.[4] The results may be seen in Table I. It can be seen that the right ventricular pressures in all dogs where overdistention is prevented (except 821 and 612) are lower than in the ones with overdistention, the average systolic right ventricular pressure being lower by 28 per cent (50/6 and 36/4 mm. Hg).

*This "Ivalon" plastic sponge derived from formalinized polyvinyl alcohol, was obtained from Ivano Inc., Chicago, Ill.

After these results were obtained, it was thought that some of these dogs would be able to tolerate a further reduction of lung tissue, especially since some of the dogs in the group with overdistention survived with only the left upper lobe remaining.

Four months after a right pneumonectomy all ten dogs were subjected to a left lower lobectomy. Intrapleural pressures were adjusted to 0 to −14 cm. water pressure, and no prothesis was used to prevent overdistention during this stage. Right ventricular pressures were studied during this procedure.

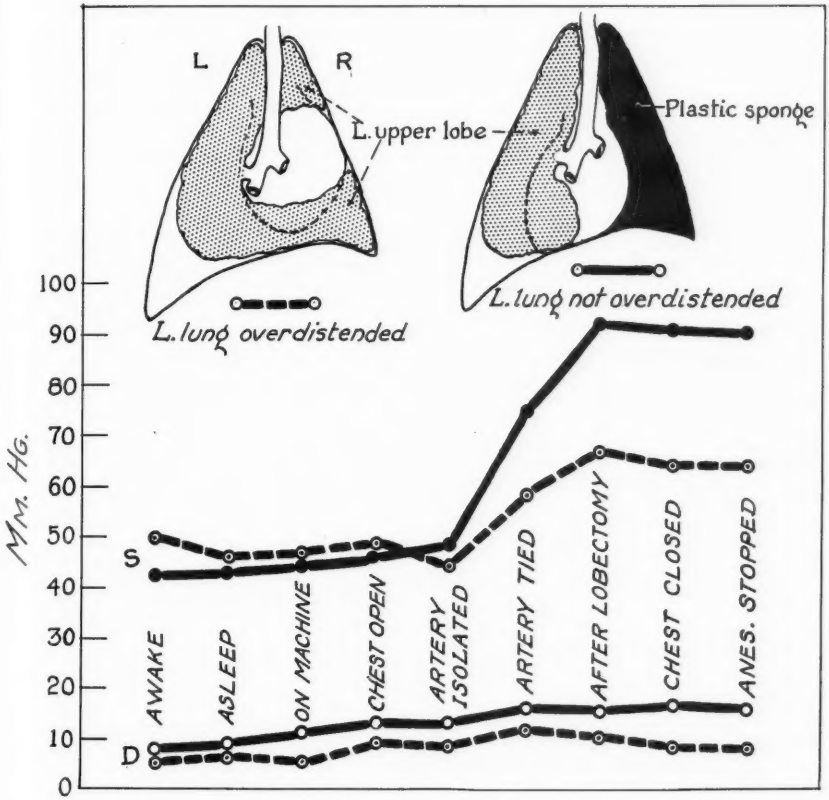


Fig. 1.—Right ventricular pressures during removal of left lower lobe in previously pneumonectomized dogs. There were fifteen dogs in the overdistended group; five survived more than three days. In the not overdistended group there were ten dogs; all died within eighteen hours. Note that in this group the systolic right ventricular pressures are much higher after ligation of the artery as compared to that of the overdistended group.

RESULTS

At this second stage it was found that at the time of ligation of the pulmonary artery branch to the left lower lobe an immediate increase in the right ventricular pressure occurred that was much higher than in the dogs of Group I where overdistention was present, as can be seen in Fig. 1 and Tables III and IV.

TABLE II. REMOVAL OF ALL LUNG TISSUE EXCEPT LEFT UPPER LOBE IN STAGES WITH OVERDISTENTION OF REMAINING LUNG TISSUE IN THIRTEEN DOGS. PERIODS OF SURVIVAL AND CAUSES OF DEATH

DOG NO.	SURVIVAL TIME	CAUSE OF DEATH
4	2 hours	Cardiorespiratory failure
36	Longer than one year	Sacrificed
379	2 hours	Cardiorespiratory failure
394	16 hours	Cardiorespiratory failure
436	1 hour	Embolus, caused by blood transfusion through cardiac catheter
437	3 days	Bronchopneumonia
486	2 weeks	Sacrificed (was in excellent condition)
593	18 hours	Cardiorespiratory failure
256	6 hours	Cardiorespiratory failure
26	1 hour	Hematoma right heart, caused by cardiac catheter
104	2 hours	Cardiorespiratory failure
999	5 weeks	Bronchopneumonia
909	14 days	Spontaneous pneumothorax

TABLE III. RIGHT VENTRICULAR PRESSURES IN MM. HG. LEFT LOWER LOBECTOMY IN DOGS HAVING PREVIOUS RIGHT PNEUMONECTOMY. OVERDISTENTION OF REMAINING LEFT UPPER LOBE

DOG NO.	DOG AWAKE	DOG ASLEEP	ON ANES. MACHINE	CHEST OPEN	ARTERY ISOLATED	ARTERY TIED	AFTER LOBEC.	CHEST CLOSED	ANES. STOPPED	LIVING OR DEAD
4	–	40/1	43/6	44/5	45/8	52/12	58/18	54/8	55/8	D
36	43/2	45/1–2	50/–2	42/4	51/3	80/9	56/9	80/2	80/0	L
379	48/4	41/5	44/6	46/12	48/12	56/15	52/6	55/6	60/9	D
394	48/8	–	48/4	42/5	48/8	76/15	86/18	73/10	74/12	D
436	48/4	34/17	40/6	34/12	41/12	54/16	90/11	70/16	63/8	D
437	53/11	58/10	52/5	38/10	36/11	42/14	72/11	63/8	64/8	D
486	63/8	59/7	53/6	43/15	46/8	60/9	63/8	68/6	63/8	L
593	–	42/2	41/5	45/6	42/5	53/8	55/8	52/9	53/8	D
Av.	50/6	46/7	46/5	42/9	45/8	59/12	67/11	64/8	64/8	

TABLE IV. RIGHT VENTRICULAR PRESSURES IN MM. HG. LEFT LOWER LOBECTOMY IN DOGS HAVING PREVIOUS RIGHT PNEUMONECTOMY. PARTIAL PREVENTION OF OVERDISTENTION OF REMAINING LEFT UPPER LOBE

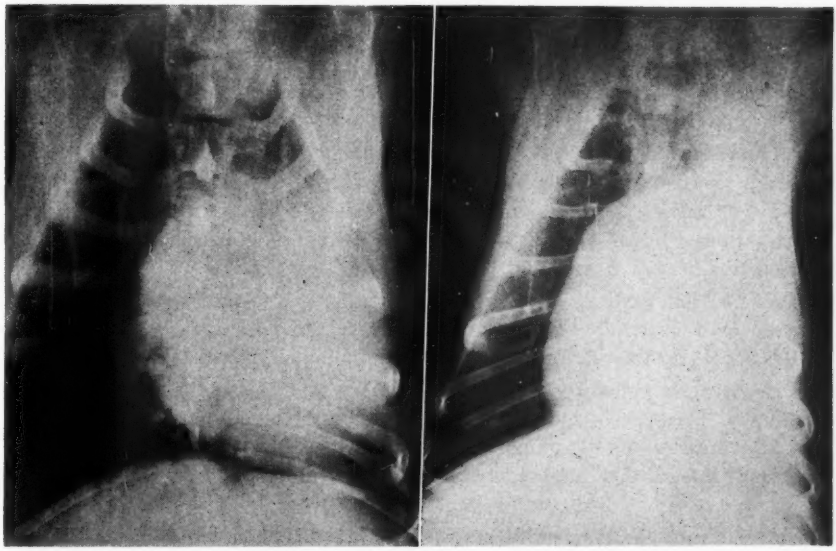
DOG NO.	DOG AWAKE	DOG ASLEEP	ON ANES. MACHINE	CHEST OPEN	ARTERY ISOLATED	ARTERY TIED	AFTER LOBEC.	CHEST CLOSED	ANES. STOPPED
821	48/4	34/17	42/6	38/8	48/12	74/16	90/11	92/16	89/10
795	42/5	45/13	45/9	50/14	56/10	78/16	100/15	95/15	92/13
815	50/7	45/5	52/6	57/9	56/9	77/11	95/12	90/13	90/14
966	39/3	30/2	30/2	30/2	30/2	44/6	67/9	67/9	67/9
602	36/7	36/7	36/5	35/6	35/6	55/9	68/6	72/4	73/4
612	78/27	78/27	74/44	60/45	68/42	120/50	135/55	145/55	141/51
362	40/15	40/15	50/15	50/15	45/15	80/15	62/10	75/15	76/15
388	35/0	35/0	42/10	50/20	50/20	70/25	130/25	100/25	100/25
534	35/3	35/3	40/5	45/10	45/10	60/15	85/10	85/15	85/15
64	19/–1	50/5	43/7	51/5	150/5	100/5	106/10	96/2	95/2
Av.	42/7	43/9	45/11	47/13	48/13	76/17	94/15	92/17	91/16

All dogs survived the operation and were placed in an oxygen box. Immediately following operation they appeared to be in fairly good condition. All of them, however, developed pulmonary edema of which they died within eighteen hours after surgery.

At post-mortem examination it was found that pulmonary edema was present in all, and acute dilatation of the right heart in some dogs. It was also found that the plastic sponge was reduced in size and was covered with fibrous tissue. It was very firmly adherent to the surrounding tissues, especially the pericardium, and was as hard as a stone. No infections were found.

DISCUSSION AND CONCLUSIONS

It is generally accepted that the resistance in the pulmonary circulation is less when the lung is normally extended as it is during inspiration. This does not necessarily mean that this is true for a markedly overdistended lung, as is the case after a pneumonectomy in a dog. The fact that the right ventricular pressure is lower where overdistention was prevented makes us believe that overdistention above a certain degree causes higher resistance and imposes a greater strain on the right ventricle.



A. *B.*

Fig. 2.—Roentgenograms of two dogs following right pneumonectomy: *A*, with subsequent overdistention of the remaining lung. *B*, right pleural cavity filled with plastic sponge to prevent overdistention. Note less shift of mediastinum, with less overdistention of remaining lung.

After this theory one would expect more surviving animals in the group of dogs where overdistention was prevented than in the overdistended group where 85 per cent lung tissue was removed and where there were four of thirteen animals surviving for longer than two weeks (Table II). The expectation was wrong, as all dogs died. The fact that there was no overdistention in this group probably is just the cause of death, the pulmonary vascular bed not having had a chance to overdistend gradually, as probably

is the case where overdistention is not prevented. (The right ventricular pressure came down after several weeks in pneumonectomized dogs where overdistention was not prevented.[4])

If, then, after a pneumonectomy the pulmonary vascular bed is again suddenly reduced by more than 50 per cent, the remaining lung tissue (left upper lobe in this experiment) does not have enough vessel capacity to transport all the blood, while in the overdistended left lung the vessels have had more chance to increase gradually in size over a longer period of time.

We believe that 50 per cent reduction of lung tissue and prevention of overdistention of the remaining 50 per cent will impose less strain on the right heart, but when further reduction of lung tissue is anticipated, overdistention might be favorable to give the remaining lung tissue and pulmonary vascular bed a chance to increase in size over a longer period of time, so that at the time of the next operation the remaining very small amount of lung tissue is able to handle the total blood flow.

Collapse of a lung by pneumothorax, prior to surgery, to be resected should enable the patient to become adjusted to the use of one lung. The beneficial effects of a pneumothorax given before a pneumonectomy in patients might partially be explained by the results of this study.

The plastic material used in this experiment is not a satisfactory type of material to use as a prothesis in the chest, since it causes too many adhesions and is too adherent to the pericardium, thus perhaps interfering with the heart action. On the basis of these experiments, it would seem to be definitely undesirable for use in patients.

Since dogs have an unstable mediastinum, a pneumonectomy will cause marked overdistention of the remaining lung. In patients, however, a more or less stable mediastinum usually prevents too much overdistention.

Bilateral lobectomy, however, might very well cause more rise in right ventricular pressure because of overdistention of the remaining lobes. Prevention of overdistention here might be of some help in hazardous cases. It is, however, well known that most young patients tolerate a bilateral lobectomy very well.

Rasmussen and associates stated in 1941 after an experimental study: "from the above findings it would appear that temporary paralysis of the diaphragm is a justifiable procedure in the human being. In bilateral operations it seems advisable that sufficient time elapse between stages for re-establishment of the diaphragmatic function and improvement of the patient's general health." To this might be added: "and adjustment of the pulmonary vascular bed."

SUMMARY

1. Approximately 85 per cent of lung tissue was removed in stages in ten dogs, while overdistention of the remaining left upper lobe was partially prevented by inserting a plastic sponge in the thoracic cavity. The right ventricular pressures were studied.

2. Prevention of overdistention of lung tissue in pneumonectomized dogs reduces the amount of elevation in the right ventricular pressure following that operation.

3. Removal of all lung tissue except the left upper lobe caused death of all dogs, while in an experiment where overdistention was not prevented some dogs survived for weeks, with only the left upper lobe remaining.

4. The plastic sponge (Ivalon) used in this experiment is not a satisfactory material to use as a prothesis in the chest, and should not be used in patients, since it becomes adherent to the pericardium and might interfere with heart action.

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TECHNIQUES OF ENDOCARDIAL ANASTOMOSIS FOR CIRCUMVENTING THE PULMONIC VALVE

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THE background and rationale for this approach to the surgical treatment of pulmonic stenosis and atresia have been reviewed in a previous publication by one of the authors. It has been pointed out that the nature and varying combination of defects in pulmonic stenosis and atresia make a direct attack on the infundibular type of stenosis less feasible than a shunting procedure.[1, 2] The latter technique provides a good outflow tract for the right ventricle with the least residual derangement in cardiodynamics. In that previous investigation, one end of an homologous vein graft was anastomosed to the distal segment of the ligated left pulmonary artery after which the other end of the graft was everted over a polyethylene tube and inserted into the right ventricle (Fig. 1). These new left pulmonary arteries remained patent for two to three weeks, and were then thrombosed. While patent, the vein valves functioned to prevent regurgitation, and the shunt delivered blood in much the same manner as the original left pulmonary artery. It has been found that homologous vein grafts substituted for an excised segment of left pulmonary artery remain permanently patent (Figs. 2 and 3). Thus, the tube anastomosis at the cardiac end of the shunt is the vulnerable portion from the standpoint of thrombosis.

Since the myocardium partially closes openings in the ventricular wall during systole, and because suture anastomoses to endocardium become obliterated, a rigid tube of some kind is necessary to hold the ventricle open and permit blood flow through the shunt.[1, 3] This rigid tube can be designed with a flare approximately perpendicular to its wall to provide immediate hemostasis when inserted into the ventricle, thus making it unnecessary to interrupt the circulation in completing the shunt. Lining the rigid tube with a vein facilitates intima to endocardial healing and presents smooth endothelium to the bloodstream. Since the initial venous-lined polyethylene tubes failed to remain permanently patent, various types of rigid tubes were substituted. It was hoped that a less reactive material might better the anastomosis in much the same manner that Blakemore, by using the relatively nonreactive vitallium, improved on Nitze's ivory rings and the magnesium

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tubes of Payr.[4-6] The types of tubes used were polyethylene, lucite, teflon, and Kel F plastics, and homologous tracheal grafts prepared in three different ways. Only the series of venous-lined tracheal and polyethylene tubes will be described in this report. The other plastics used with and without venous lining will be alluded to briefly but described in detail in another publication.

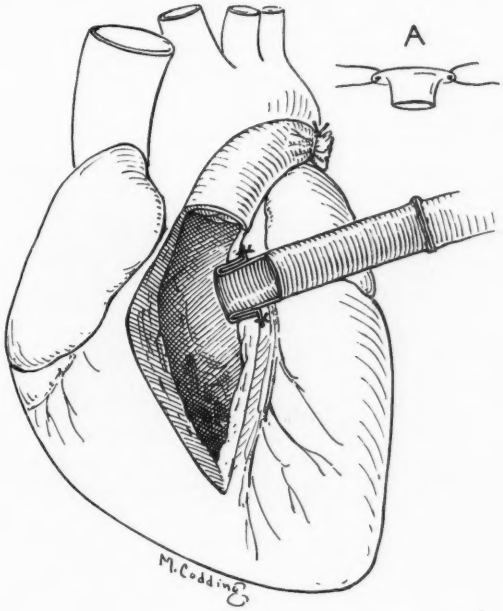

Fig. 1.—Cross section of venous-lined tube in the right ventricle. Left pulmonary artery is ligated just beyond the bifurcation of main pulmonary where right pulmonary artery courses under aortic arch. Distal left pulmonary artery is sutured to the homologous vein graft as depicted. Insert *A* shows the plastic tube without vein graft.

MATERIALS AND METHODS

Preparation of the Vein Grafts.—The grafts were abdominal cavae excised from the liver to below the renal veins. The donor dog was less than two hours post mortem, and about 3 kg. heavier than the recipient, of similar nutritional status, in order to match the graft and the left pulmonary artery at the suture anastomosis and to avoid stretching or "funneling" at the tube anastomosis. The veins were taken with aseptic precautions and stored for periods up to seventeen days in solution I at 0° to 10° C.*

Preparation of the Tracheal Tubes.—The tracheas of recently sacrificed dogs were excised 1 cm. above the carina and a few millimeters below it on the right- and left-main stem bronchi. The medial walls of the bronchi were excised, leaving a semiflexible flare at one end

*Solution I consists of 85 per cent balanced salt solution, with bicarbonate buffer and phenol red indicator, homologous serum 10 per cent, and antibiotics 5 per cent. The formula for balanced salt solution, which is similar to Tyrode's solution, can be found in the publication of Pierce and associates.[7] The antibiotics in the above solution were penicillin 400 units per cubic centimeter, streptomycin 2 mg. per cubic centimeter and sulfadiazine 0.12 mg. per cubic centimeter. Sulfadiazine was added to insure the sterility of the tracheal grafts stored in Solution I. For the vein grafts taken with aseptic technique, the antibiotics were probably superfluous.

of the tube of trachea. The donor was selected about 6 kg. smaller than the recipient dog to match the trachea with the donor vein (chosen as described previously) and to provide an ample stoma in the heart wall. The tracheal grafts were prepared in three ways. The first group was immersed in a solution of 90 c.c. isotonic saline and 10 c.c. of 40 per cent neutral formalin. After three to twelve hours they were stored in the same solution diluted ten times. Twenty-four hours before operation they were washed repeatedly in sterile distilled water to remove all but the protein-bound formaldehyde. The second group of tracheas was mechanically cleaned with phisoderm and G-11 and after thorough rinsing immersed in a solution of 80 c.c. of balanced salt solution buffered with 1.4 per cent bicarbonate and 20 c.c. of 1:1000 zephiran and stored in a refrigerator at 0° to 10° C. The third group was mechanically cleaned with the phisoderm and G-11 mixture and stored at 0° to 10° C. in Solution I, the solution used to preserve the vein grafts.

Portions of the tracheal and venous grafts were taken for bacteriologic study, while other specimens were incubated in tissue culture medium to determine preoperative viability. Each bacteriological specimen was thoroughly washed in sterile distilled water to remove antiseptics and antibiotics.

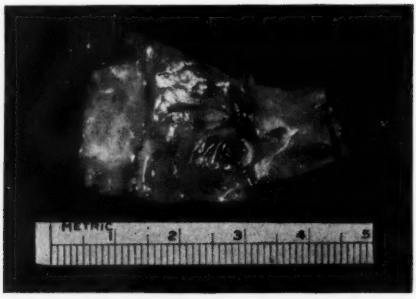

Fig. 2.—A segment of homologous vena cava substituted for an excised segment of left pulmonary artery. Proximal suture line is at one centimeter on the ruler; distal anastomosis at three centimeters. Note smooth endothelial lining of the graft and suture lines at twenty-seven days postoperatively.

Preparation of the Polyethylene Tubes.—Stock tubing of 11 mm. inside diameter and 12.5 outside diameter was cut into lengths of 14 mm. and one end flared with a hot die. A few millimeters from the opposite end a groove was made around the circumference. The effective length of the tube from this end to the flare was about 10 mm. or 12 to 14 mm. including the flare. The tubes were sterilized in 1:1000 aqueous zephiran for eighteen hours prior to operation.

Operative Technique.—The animals were premedicated with 0.6 mg. of atropine sulfate and anesthesia induced with sodium pentothal intravenously. Two polyethylene tubes were inserted through a size 14 needle into foreleg veins and used for subsequent injections of blood, dextrose, or cardiac drugs.[8] A rubber tube which fitted a little loosely was inserted into the trachea and connected to an Erlanger pump. The latter supplied compressed air and ether with valves to modify rate and depth of respiration, the relative lengths of inspiration and expiration, and the concentration of ether in the mixture.

The dog was placed midway between the supine and right lateral positions. The fourth left intercostal space was opened from the sternum to the tip of the scapula, and the fifth rib divided at the sternal junction and under the tip of the scapula. The left pulmonary artery, freed from the hilus of the lung to the bifurcation, was clamped near the hilus and ligated close to the bifurcation. The artery was then divided close to the ligature and cuff reinforced with a suture ligature. The distal segment was irrigated, stripped of adventitia, and the end cut on the bias when the vein graft appeared slightly large. The graft which had been fixed to the tracheal or plastic tube was anastomosed with a continuous everting mattress suture of

00000 arterial silk or chromic catgut to the distal end of the divided left pulmonary artery. Retrograde bleeding and saline irrigations were used to test the anastomosis and vein graft for leaks (Fig. 1).

The pericardium was then opened along the interventricular septum with a short perpendicular extension to the tip of the right auricle. The right edge of the pericardium was marsupialized with several pericardial sutures to rotate the right ventricle to the left of the partially overlying sternum. Four epicardial sutures of 00 cotton were then spaced on the sides of a rectangle running from the pulmonary conus 2 cm. down the ventricular wall and about 1 cm. from the septum. Each of the four sutures was spaced equally through the flare of the tube or trachea in the appropriate position to provide hemostasis and prevent twisting of the vein graft. If the flare or tube was larger than usual a fifth epicardial suture was placed parallel to and just below the pulmonic valve perpendicular to the planes of the other stitches. This suture was removed if the other four provided complete hemostasis.

Fig. 3.—Another control graft interposed in left pulmonary artery. Graft was purposely made redundant in length but despite angulation was fully patent at autopsy fourteen months postoperatively. Angiocardiogram is 9.5 months postoperatively. Arrow points to proximal anastomosis partially obscured by tracheal shadow.

In the first half of the series a Bard-Parker blade was used to make the opening into the ventricle. The only two deaths during operation in the series were due to excessively large incisions in the heart. New blades of various widths were therefore designed with a cutting edge on the end of the blade almost perpendicular to the handle and pointed with a central angle of about 115 degrees.* By inserting the blade of proper width perpendicular to the heart wall, an incision could be made 2 to 3 mm. larger than the tube diameter which would permit the introduction of the tube into the ventricle without resistance and with complete hemostasis following insertion. With proper performance of the heart anastomosis, blood loss, and trauma were so slight that no grossly perceptible change in contractility or blood pressure occurred. If the blood loss was more than 50 c.c. it was quantitatively replaced through the polythene tubes as rapidly as the heart would accept it without dilatation or diminished contractility. If contractility decreased seriously, 10 c.c. of 50 per cent glucose

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was given intravenously followed by 0.5 c.c. of a solution of 1 c.c. of 1:1000 adrenalin in 10 c.c. of 1 per cent procaine. If this dose given intravenously did not improve contractility, another 0.5 c.c. of the mixture was given into the right auricle. If the adrenalin procaine solution had to be given again later, another injection of 50 per cent glucose was made and maximal aeration of the lungs obtained to prevent ventricular fibrillation. If ventricular

TABLE I. SERIES OF OPERATIONS IN SUMMARY FORM

DOG NO.	TUBE IN HEART ANASTOMOSIS	LENGTH OF SURVIVAL	CAUSE OF DEATH	CONDITION OF DOG	CONDITION OF SHUNT		
					AT OPERATION	POSTOPERATIVE ROENTGENOGRAMS	AT AUTOPSY
1	Formalin Trachea	7.3 months	Sacrificed	Excellent	2+	–	0
2	Formalin Trachea	4.5 months	Sacrificed	Excellent	2+	–	0
3	Formalin Trachea	4.5 months	Sacrificed	Excellent	3+	68 days—0	0
4	Zephiran Trachea	6.9 months	Sacrificed	Excellent	4+	36 days—0	0
5	Zephiran Trachea	Operative death	Hemorrhage	–	–	–	–
6	Zephiran Trachea	Operative death	Hemorrhage	–	–	–	–
7	Zephiran Trachea	8 days	Pneumonia	–	2+	–	0
8	Zephiran Trachea	3.5 months	Sacrificed	Excellent	3+	14 days—0	0
9	Zephiran Trachea	6 days	Pneumonia	–	3+	–	4+
10	Solution I Trachea	3.5 months	Sacrificed	Excellent	4+	22 days—4+ 43 days—0	0
11	Solution I Trachea	5.6 months	Sacrificed	Excellent	4+	29 days—2+ 37 days—0	0
12	Solution I Trachea	2.6 months	Sacrificed	Excellent	3+	28 days—4+ 34 days—4+ 43 days—3+ 59 days—0	0
13	Solution I Trachea	2.6 months	Sacrificed	Excellent	3+	28 days—0	0
14	Polyethylene	27 days	Sacrificed	Distemper	4+	–	2+
15	Polyethylene	1.3 months	Sacrificed	Excellent	4+	21 days—0	0

Under "condition of shunt" 4+ denotes maximal filling, 3+ indicates good filling of a fully patent shunt, 2+ represents definite obstruction to filling, 1+ denotes marked obstruction and 0, complete occlusion of shunt.

TABLE II. RESULTS OF TREADMILL STUDIES ON SECOND TRIAL OF DOGS STOPPED WELL SHORT OF MAXIMUM EFFORT

DOG NO.	POSTOPERATIVE INTERVAL	TYPE OF CARDIAC TUBE	DEGREES OF INCLINATION OF TREADMILL	SPEED (M.P.H.) OF TREADMILL	TIME ON TREADMILL IN MINUTES	CONDITION IMMEDIATELY AFTER RUN
1	3.8 months	Formalin Trachea	10	4.2	17	Pulse 128. Frisky
8	2.5 months	Zephiran Trachea	10	4.2	32	Pulse 136. Strong
11	2.0 months	Solution I Trachea	10	4.3	19	Running easily
15	24 days	Polyethylene	10	4.3	20	Running well but pulse 160 and panting rapidly

Although dog number 15 was too early postoperatively to have developed full strength or abundant collateral circulation through the bronchial arteries, he ran well without signs of exhaustion.

fibrillation supervened, manual massage was instituted until the heart could be shocked into asystole with a 1 to 1.5 ampere current and the above measures instituted to restore contractility.[9]

The chest was closed in layers with careful attention to the expansion of the left lung and the removal of intrapleural air through catheter suction during closure. If the breath sounds were diminished following closure, the pleural space was aspirated with a needle, and if they were associated with râles and rhonchi the trachea was aspirated and, if necessary, bronchoscopy performed. Crysticillin was given for a few days postoperatively.

Postoperative Observations.—Angiocardiography was performed at intervals postoperatively to determine patency, and function of the graft and treadmill studies were used to evaluate the general cardiopulmonary function. The animals were sacrificed under nembutal and histologic study made of the significant gross changes at autopsy.

Fig. 4.—Dog No. 12 on the thirty-fourth postoperative day. A similar film was obtained on the forty-third day. Air in the trachea partially obscures the graft (arrow), but patency of the shunt and filling of the left pulmonary arterial tree are evident.

RESULTS

Toleration of the Operative Procedure.—Table I summarizes the results of fifteen operations. The two deaths during operation occurred before the use of special heart knives to control the size of the heart incision. The two other deaths were about one week postoperatively from atelectasis and pneumonia. Both followed anesthesias characterized by profuse mucous secretions and diminished respiratory excursions during and immediately after operation. Preoperative atropine and, if necessary, postoperative suction or bronchoscopy have eliminated this complication in forty subsequent cardiac operations. The operative mortality in this series including the anesthetic complications would be 27 per cent, while the mortality from the cardiac procedure per se would be 13 per cent.

Long-term follow-ups on the surviving animals demonstrated no detectable sign of cardiac dysfunction. Four animals (numbers 1, 8, 11, and 15)

were run on the treadmill. The second time on the treadmill the animals ran at a 10-degree incline, and at 4.2 m.p.h. for periods within the range of a normal dog without signs of exhaustion[10] (Table II).

Function of the Vein Grafts.—Table I shows the condition of the shunt at operation on various postoperative days and at autopsy. All the grafts with the exception of dogs 1, 2, and 7 filled well at operation, giving a pink lung and normal pulsations in the distal left pulmonary artery. The filling of the grafts in dogs 1, 2, and 7 was diminished because of tubes too short, too narrow, or only partially through the ventricular wall. All the grafts, however, were occluded at autopsy with the exception of the two animals that died on the sixth and twenty-seventh postoperative days. Roentgenograms taken at various postoperative intervals showed one shunt open at forty-three days postoperatively (Fig. 4). Although some grafts were open at three weeks, most were closed before the end of the fourth postoperative week.

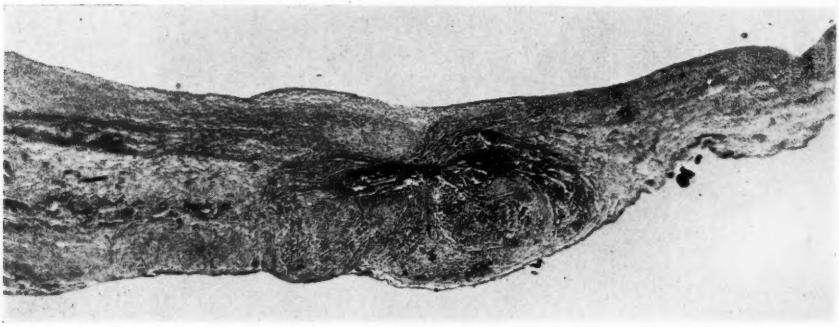

Fig. 5.—Photomicrograph of the suture anastomosis of dog No. 14 on the twenty-seventh postoperative day. Note endothelioid lining of the graft and granulomatous response to arterial silk, especially on the narrow or graft side of the anastomosis.

Autopsy Findings.—In all cases, except the two that died of pneumonia, the lungs were pink, crepitant, and expanded. The two exceptions had partially collapsed and consolidated left lungs which sank in water. Microscopically they showed pneumonia and some agonal pulmonary edema. The left lungs were almost always adherent to the intercostal incision, the pericardium, and the graft. There was no detectable difference between the reaction to various types of preserved trachea and to the pure polyethylene tubes.[11, 12]

The vein grafts from dogs more than three months postoperative were shrunken, and the walls apposed. The graft, patent at autopsy six days postoperatively in dog No. 9, showed the early host inflammatory reaction in the adventitia. The donor endothelium had disappeared and the reconstruction of the intima had hardly begun. This left bare areas of subendothelial connective tissue in contact with the blood stream.[13] This surface, on gross examination, looked reddish and had tiny clumps of fibrin in various areas of the graft. The vein graft in dog No. 4, patent at autopsy on the twenty-seventh postoperative day, showed no fibrin deposition macroscopically, and a firm intimal union at the suture anastomosis on microscopic study. The intima became thinner

towards the middle of the graft, but was lined for the most part with smooth endothelioid cells. The round-cell inflammation of the adventitia had almost completely subsided without as yet much fibrous tissue reconstruction. The lack of fibroplasia in the adventitia and media plus the disappearance of donor tissue in these layers left the wall thin at this stage of healing (Fig. 5). The endocardial end of this shunt was typical of most of the venous-lined plastic tubes, as reported previously.[1] Just inside the intraventricular portion of the tube a fibrous constriction of the vein graft reduced blood flow to a minimum and would have produced thrombosis distally in a few days (Figs. 6 and 7). Histologic sections of this area showed serosanguineous exudate between the

A.

B.

Fig. 6.—*A*, Endocardial, and *B*, epicardial views of the shunt in dog No. 14, twenty-seven days postoperatively. The typical fibrous constriction of the graft just inside the tube has narrowed the lumen to about 3 mm. in that area and would have precipitated thrombosis in a few days. Note well healed suture anastomosis.

adventitia of the lining vein and the inner surface of the plastic tube. In addition to the marked proliferation of connective tissue, there were small areas of necrosis and hemorrhage scattered throughout this portion of the graft wall suggesting continual trauma.

The rate at which the host destroyed the tracheal grafts varied widely and for the most part pari passu with the degree of reaction around the silk sutures. Although the grafts prepared in formalin had slightly thinner and more rigid walls, destruction of the fibromuscular tissue between the tracheal rings deformed all the grafts during the first two months postoperatively, causing gradual collapse and, in a few, extrusion from the ventricle. This extrusion from the ventricle did not occur with the plastic tubes—patent or thrombosed. The destruction and removal of the cartilaginous rings was notably slow and incomplete at six months or even longer. The cartilage cells in the lacunae were shrunken or absent from the outset. The lacunae became closely packed and confluent as the matrix degenerated and disappeared. This left large holes containing the basophilic residue of cartilage undergoing phagocytosis by lymphocytes and macrophages. In other areas, round-cell invasion and isolation of small fragments of cartilage was followed by organization of the acellular matrix by fibrous tissue.

Bacteriologic and Tissue Culture Studies.—The tracheal tubes prepared with formalin and zephiran were, of course, sterile and nonviable. Tracheal tubes mechanically cleaned with phisoderm and G-11 soap and immersed for two or more days in Solution I were likewise free of bacterial growth. Bacteriologic cultures of the latter group of tracheal specimens were positive in the few specimens studied, if either the phisoderm and G-11 washing or the immersion in Solution I was omitted. Veins taken aseptically and stored in Solution I were found to be sterile.

Vigorous fibroblast proliferation could be seen in tissue cultures of one- and two-week-old veins. Veins three weeks or more in Solution I failed to show growth in tissue culture. No tracheas prepared in the three ways previously described grew in tissue culture. One specimen of trachea washed in water and kept in Solution I for ten days showed moderate growth.

DISCUSSION

In the previous report it was noted that the dogs that emerged from anesthesia invariably tolerated the new shunt well—patent or occluded. The operative mortality in those initial experiments was about 50 per cent, although the brevity of the series and the continual change in operative technique made this figure an approximation. Although the technique is still changing, the operative mortality in this series is a definite improvement over that reported earlier. The anesthesias in the initial series were intravenous nembutal supplemented by a mechanical respirator which delivered 100 per cent oxygen but did not eliminate the positive pressure during the expiratory phase and permit adequate collapse of the lungs. In several instances, the resulting hypercapnia and decreased ventricular filling were sufficient to cause death before the anastomoses were attempted. In other operations it caused excessive medi-

astinal and diaphragmatic motion, thus prolonging the operation as well as lowering the myocardial reserve. With intermittent positive pressure air or oxygen fully expanding and collapsing the lung at a rapid rate, the mediastinum and diaphragm can be kept almost motionless on a light ether anesthesia. This supports myocardial function and facilitates the anastomoses greatly.

The insertion of the intracardiac tube can be done without significant blood loss or trauma if the opening in the heart is the proper size, i.e., 2 to 3 mm. longer than the outside diameters of the tubes. If the knife described previously is sharpened regularly and inserted carefully perpendicular to, and

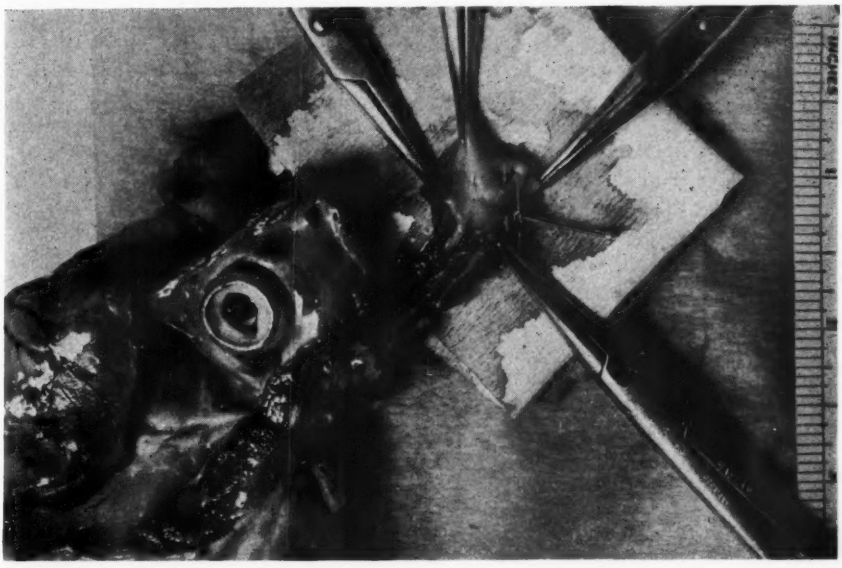

Fig. 7.—The shunt in dog No. 15, 1.3 months postoperatively. The thrombus extends from the constricted area of the graft distally to within one centimeter of the barely visible catgut suture anastomosis. The beginning shrinkage of the graft is typical but the clot usually propagates to and involves the silk suture anastomosis.

completely through the heart wall, the length of the incision in the endocardium should be about the same as the width of the knife blade. With four or five epicardial sutures spaced properly with both ends through the tube flare, hemostasis is assured even when the heart incision is slightly large. The use of No. 00 cotton assures tight ligation of these epicardial sutures without breakage.

Except for the two animals that died of postoperative atelectasis and pneumonia and another animal with distemper, all the animals surviving the operative procedure were healthy and well. The treadmill studies in these animals corroborate the previously reported electrocardiographic, roentgenographic, and other evidence of normal cardiac function in the presence of the

intracardiac tube and graft. Even without training, conditioning, and maximal effort the animals did an amount of work incompatible with cardiac decompensation or any marked lowering of myocardial reserve.

The failure of these shunts to remain permanently patent is due to two principal factors: (1) the lack of sufficient pressure gradient on ligation of the left pulmonary artery, and (2) the intrinsic weakness of the venous-lined tube used in the heart anastomosis. It is well established that after ligation of one pulmonary artery, the blood flow is shunted to the opposite lung without significant or prolonged elevation in main pulmonary artery pressure.[14] The development of collateral circulation through the bronchial arteries to the distal left pulmonary artery per se elevates the left pulmonary artery pressure to half of the normal value, further dissipating the pressure gradient and the volume flow through the shunt.[1, 15, 16, 17] It has been shown that the Blakemore type of anastomosis is inferior to suture anastomosis in preventing thrombosis, especially in anastomoses with low pressure gradients.[18-21] When the venous-lined tube is placed in the ventricle, the brunt of the stretching force of each systolic ejection is transmitted to the fixed portion of vein graft near the point of eversion over the end of the tube. This area of tension thickens and progressively restricts flow until thrombosis occurs just beyond the constriction and propagates distally to the suture anastomosis. Another factor favoring constriction of the tube in this area is the collection of serosanguineous exudate in the space between the adventitia of the lining vein and the inner surface of the rigid tube. In the venous-lined tracheal tubes, the gradual distortion and destruction of the tracheal graft by host reaction is enough per se to occlude the heart anastomosis.

It is possible to obviate these deleterious factors by attaching the vein graft to the outer end of the tube. By using various smooth and water repellent plastic surfaces for the intracardiac portion of the shunt, it has been possible to ligate the main pulmonary artery and permanently divert the entire cardiac output through the shunt without clotting or untoward changes in the cardiac function. This work is being reported in another publication.

SUMMARY

A series of fifteen attempts at constructing a new left pulmonary artery with venous-lined tracheal and polyethylene tubes resulted in eleven survivals which remained healthy and well with the exception of one animal with distemper. There were two operative deaths from hemorrhage and two postoperative deaths from atelectasis and pneumonia. These deaths are considered preventable in the light of present knowledge and refinements of operative technique. Four animals ran on the treadmill at a 10-degree incline for distances within the range for normal animals.

Angiocardiography demonstrated good filling of some shunts as long as forty-three days postoperatively, but the majority of shunts were occluded by the third or fourth week. The factors causing these thromboses have been analyzed, and other types of endocardial anastomoses devised which obviate these factors.

CONCLUSIONS

1. With attention to principles mentioned herein, a new left pulmonary artery may be constructed in the normal dog with a vein graft and a rigid intracardiac tube with a low operative mortality.

2. The animals surviving the operation will remain healthy—with or without patency of the shunt.

3. With venous-lined tubes of homologous trachea or polyethylene, the shunts eventually became occluded. This usually occurs during the third or fourth week postoperatively.

4. The factors causing this thrombosis have been analyzed and described.

The authors wish to express appreciation to Miss Elnore Hitchcock for assisting in the operative procedures. They are also grateful to Dr. John Hanks for his advice and help in the preservation of the various grafts and in testing their viability in tissue culture. Mr. Rudolph Beaver has kindly supplied the heart knives.

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FIBROSARCOMA OF THE DIAPHRAGM

Report of a Case

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PRIMARY tumors of the diaphragm do not occur frequently. A survey of the literature[1-35] disclosed thirty-eight fully substantiated cases of diaphragmatic tumors, including the present case, of which sixteen were classified as benign, while twenty-two were malignant (Table 1). The benign tumors, fibromyomas and lipomas, are the most common, while fibrosarcoma is the most often-reported malignant tumor.

Of the tumors described as benign, those of Kinsella[26] and those of Bonamy,[25] closely resemble the benign phase of the case herein described. Kinsella[26] reported a 2-pound fibromyoma from the anterior portion of right hemidiaphragm, occurring one-half above and one-half below the diaphragm, and resembling fibromyoma of the uterus grossly. Bonamy[25] reported 1,200 Gm. of fibromyomas arising from the right side of the diaphragm, with one large tumor and four smaller ones. Recovery followed the surgical treatment in both of these cases. Gale and Edwards[12] suggest that the tumor described by them as "primary endothelial sarcoma" might be benign, and reported that histologic opinions obtained from several competent pathologists varied widely. This is not an uncommon experience, and illustrates that it is admittedly difficult in special cases to draw a sharp line between malignant and benign tumors of the diaphragm.

The patient's history and clinical course aids in making a diagnosis of a mass in the region of the diaphragm. Tumors of the diaphragm caused chest pain in ten of the cases, abdominal pain in one, and related pain in another. Fullness in the lower chest precedes or accompanies dyspnea, especially upon exertion. Edema occurs if there is embarrassment of the heart in advanced cases.

CASE REPORT

This patient, a white man, aged 60 years, occupation farmer, experienced three attacks of illness in the last ten years, all somewhat similar, but differing in several details. Upon admission, the chief complaint was pain and fullness of the left chest, shortness of breath, and edema of feet and ankles.

The first attack occurred in 1938 when he was suddenly struck by momentary stabbing pains recurring every few minutes, beginning in the abdomen rather deeply, but anteriorly, in the left anterior axillary line approximately one-half distance between the costal margin and iliac crest, and migrating rapidly up the left side of the chest, over the left shoulder, and then down the left posterior chest to reach the point of origin. This attack covered a one-week period. Later pains became worse with deep breathing, and severe pain tended to center in the "heart region." He doubted his ability to survive the next pain. Shortness of breath rapidly developed, and was especially aggravated by exertion. At the onset he took

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strong physic with whiskey for a "stimulant," and the resultant caused fullness in the left chest. Physics such as salts or castor oil were taken every six to eight weeks. He described the sensation of fullness during the first attack "like brickbat in the side, one-half brick high and one brick sideways (lateromedially)," clearing with slight change in position, thereby relieving pain and permitting him to recline. This sensation upon change of position occurred throughout his first attack.

The second attack, in 1941, was of one week's duration. While shucking corn, pain appeared in the same location, but migrated to the left sacral area. Pain was characterized as more continuous and less severe, but was still stabbing in character and required bed confinement. Pain was aggravated in attempting to get out of bed.

The third attack occurred in 1948. While sitting in church he was seized with a sharp, hard pleurisy pain under the left shoulder blade, passing through to the front of the chest. It was worse upon deep breathing. Rubbing liniment was prescribed, and the pain shifted to the location originally described in first attack, left anterior axillary line midway between

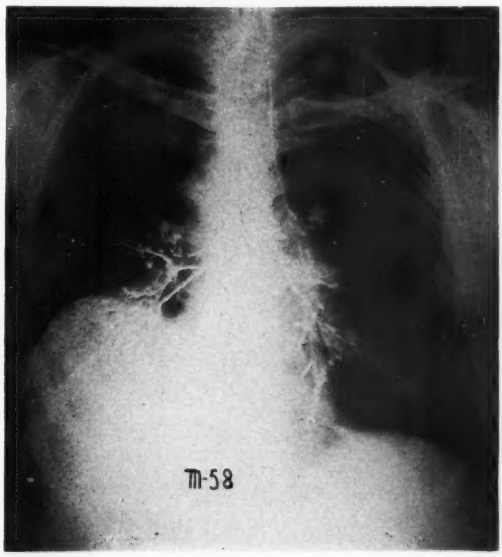

Fig. 1.—Bronchogram shows extrapleural density in left chest displacing bronchi.

the left costal border and left iliac crest, and situated moderately deep. After the shift in location of pain, some relief was experienced. At this point, the patient described "vibration and blubbering" like fluid in the left chest, changing position with posture and motion. Later on, edema of the feet and ankles was noticed, and a roentgenogram of his chest was advised.

Past history is negative for any serious illnesses, accidents, or operations. In his family history, his mother had died in 1904 with tuberculosis.

Positive findings of physical examination consisted of: left pupil slightly irregular; nasal septum deviated to the left with partial obstruction; thorax symmetrical with restricted respiratory movements, along the right margin; the right lung exhibited increased breath sounds; the left lung presented dullness at the base, especially anteriorly, with absent breath sounds and absent fremitus at the base anteriorly; axillary fremitus was heard on the left side.

Laboratory findings were: W.B.C. 10,900; juveniles 1 per cent, stabs 1 per cent, segmenters 80 per cent, small and large lymphocytes 18 per cent. Sedimentation rate 10 mm.

(Cutler method). Urinary findings were negative. R.B.C. 4,000,000, with 76 per cent Hb. (Sahli). Blood type A. Aspirated bronchial secretions were cytologically negative for neoplastic cells.

X-Ray Findings.—Bronchogram (Fig. 1) demonstrated a dense mass in the left lower chest reaching the level of the ninth rib and displacing the left lower bronchi superiorly and the heart slightly to right. Fig. 2 is a radiograph taken on the sixth postoperative day. The diaphragm is outlined. A small quantity of fluid is present.

Operative Report.—A large, rounded, well-encapsulated mass was located on the left diaphragm with major fibrous attachment in the form of a short pedicle located posterocentrally in an area about 4 by 3 cm. and which mass, when separated, left bleeding surfaces on both diaphragm and tumor capsule. Pleural adhesions were present laterally and medially connecting to diaphragm and to mediastinum. There were large adhesions connecting the

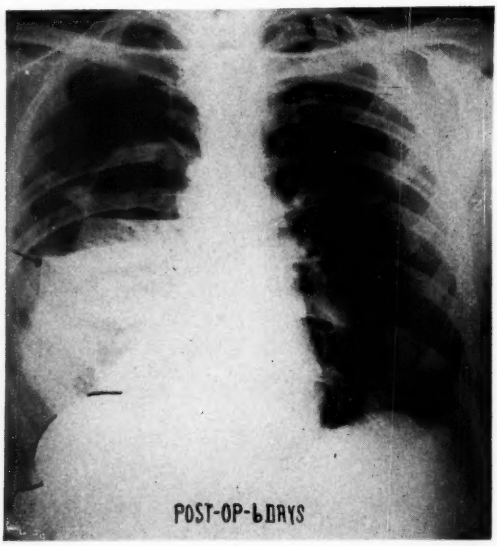

Fig. 2.—Radiograph taken six days after removal of tumor shows outline of left diaphragm, small quantity of fluid, lung re-expanding.

tumor firmly to the inferior aspects of the lung which appeared and felt atelectatic. The tumor was well demarcated and encapsulated. Recovery was uneventful. The patient was discharged from the hospital on the sixth postoperative day.

Gross Pathology Report.—Tumor mass (Fig. 3) measured 15 by 10 by 10 cm. and weighed 190 grams. Surface was smooth except for areas of pleural and diaphragmatic attachment and a bosselated area approximately 4 cm. in diameter. Consistency was moderately firm and resilient and cut surface exhibited bulging with occasional yellowish degenerated areas, tumor being similar in gross characteristics to uterine leiomyomas. It was circumscribed and encapsulated.

Microscopic Description.—(See Figs. 4 and 5.) Section showed tumor composed of solid masses of spindle cells. There was a moderate amount of intercellular substance. The nuclei were very numerous. They were of moderate size and of uniform staining. The chromatin was evenly dispersed. Mitoses were rare. There was no special architectural arrangement beyond tendency of cells to form thick bundles. These cells did not appear especially active.

TABLE I

MALIGNANT		BENIGN	
Sarcoma:			
Fibrosarcoma[1-5] (present report)	6	*Lipoma:*[20, 21, 22, 23]	4
Fibromyosarcoma[6]	1	*Fibroma:*	
Neurofibrosarcoma[7]	2	Fibroma[24]	1
Rhabdomyosarcoma[8, 9]	2	Fibromyoma[25, 26]	2
Leiomyosarcoma[10]	1	Rhabdomyofibroma[27]	1
Myosarcoma[11]	1	Angiofibroma[28]	1
Undifferentiated Myosarcoma[10]	1	Neurofibroma[29]	1
Endothelial Sarcoma[12]	1		
Round Cell Sarcoma[13]	1	*Lymphangioma:*[30]	1
Mixed Cell Sarcoma[14]	1		
Sarcoma[15]	1	*Chondroma:*[31]	1
Undifferentiated Sarcoma[16]	1	*Dermoid cyst:*[32]	1
Endothelioma:		*Cystic tumor:*[33, 34, 35]	3
Fibroangioendothelioma[17]	1		
Hemangioendothelioma[18]	1		
Mesothelioma[19]	1		
Total	22	Total	16

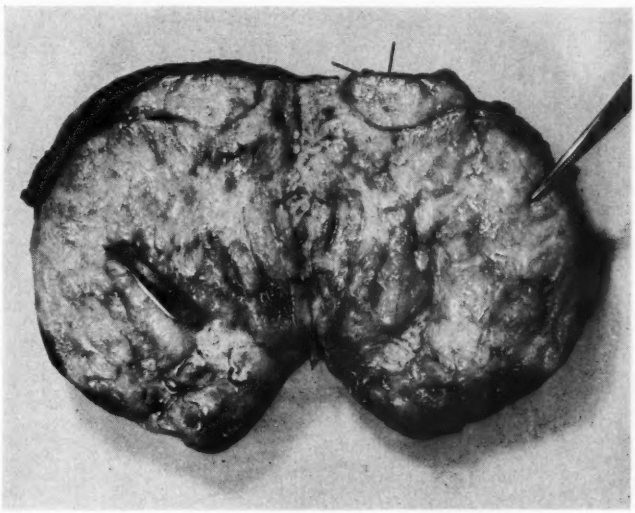

Fig. 3.—Hemisection of tumor. Blade points to yellowish degenerated area.

The tissue appeared to be benign. Other portions of tissue were somewhat distorted. One area contained many capillary-sized spaces formed of cells similar to those of tumor, and here the fibrous nature of the tumor was not so marked.

Subsequent Course.—The patient remained symptom-free, with apparent recovery, for one year. Then symptoms began to recur, finally leading to biopsy of recurrent tumor mass in June, 1950. This tumor was seen to be larger than a cocoanut, of softer consistency, red in color, with increased vascularity as compared to the first tumor. Attachment was extensive and confined within the medial half of the diaphragm with definite invasion of that structure, whereas the original tumor did not invade the diaphragm. The microscopic picture (Fig. 6) was also different with varying degrees of fibrosarcomatous activity in various areas. There were no areas as inactive and benign in appearance as was the original tumor. It was considered inoperable on exploration. A biopsy showed the tumor to be a malignant fibrosarcoma. Following deep x-ray therapy, the size of the tumor was not greatly altered, but

the patient apparently was more comfortable. Subsequent radiograph (Fig. 7) showed the recurrence of the diaphragmatic tumor mass, with metastases to both lungs. The patient died thirty-four months after removal of the initial tumor.

COMMENT

It is perhaps idle to speculate whether these were two separate tumors, or the second one a recurrence, with malignant degeneration of the original tumor. We might assume the original tumor to be a histologically and ap-

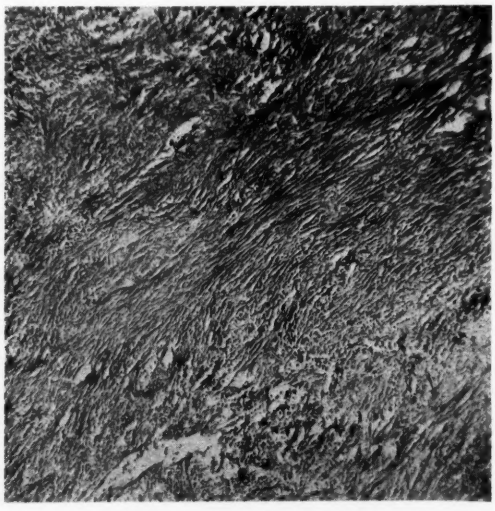

Fig. 4.

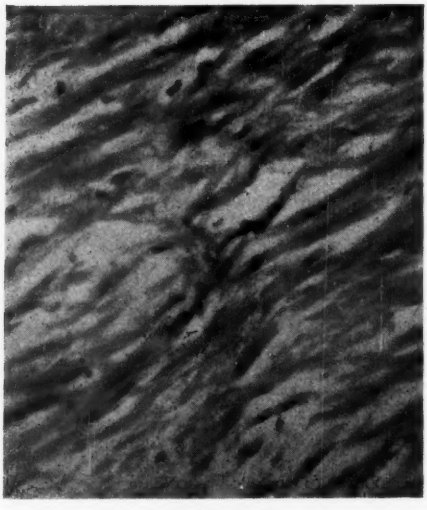

Fig. 5.

Figs. 4 and 5.—Photomicrographs showing low (×60) and high (×530) magnification, the inactive phase.

parently benign leiomyofibroma of the diaphragm which underwent malignant anaplasia and degeneration in its recurrence in the form of fibrosarcoma. The original tumor, however, was probably a low-grade fibrosarcoma, which became anaplastic and activated in its recurrence.

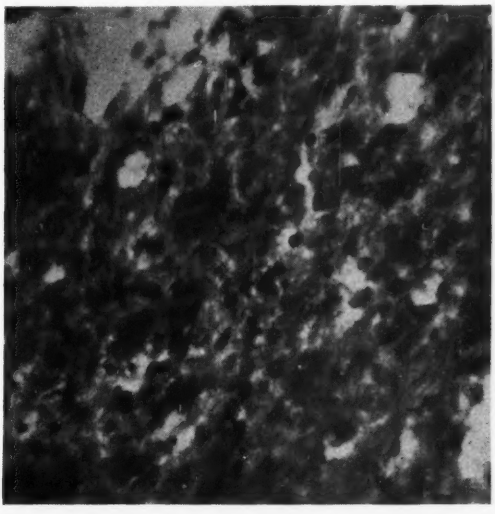

Fig. 6.—Photomicrograph (×530) demonstrating marked change and fibrosarcomatous activity of the recurring tumor.

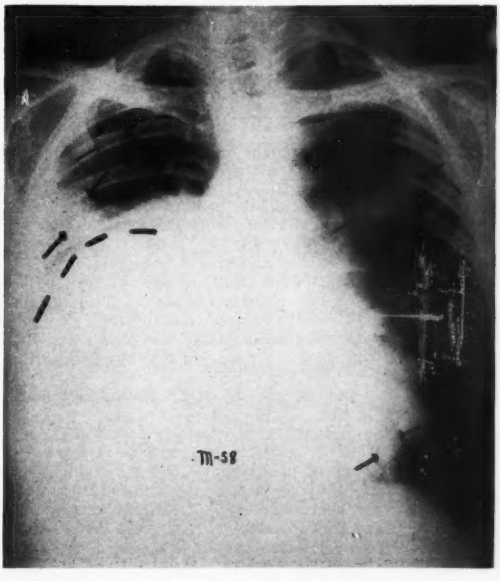

Fig. 7.—Radiograph thirty-three months after removal of initial tumor, showing the recurrence in the diaphragm with metastases.

SUMMARY

1. A case of fibrosarcoma of the diaphragm is presented.

2. A review of the literature revealed thirty-eight primary tumors which have occurred in this anatomic location.

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THE REPAIR OF EXPERIMENTAL TRACHEAL DEFECTS WITH FRESH AND PRESERVED HOMOLOGOUS TRACHEAL GRAFTS

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IN 1940 Taffel[1] described the regenerative capacity of the trachea and several reports have appeared subsequently in the literature concerning experimental resection of the trachea in dogs.[2-7] A few reports of attempts to restore the continuity of the human trachea have been recorded.[8-10]

It is conceivable that situations that make bridging of defects in the trachea desirable may arise in dealing with neoplasms, inflammatory stenosis, or trauma in the cervical or thoracic trachea. One difficulty complicating anastomosis of the larger respiratory passages is the frequent development of strictures postoperatively. At this writing no reports describing the use of tracheal grafts to repair large tracheal defects could be found in the available literature.

Preliminary experiments were performed on the cervical trachea of anesthetized dogs in order to compare various methods of preservation and insertion of tracheal grafts. All tracheal grafts were obtained by clean, but not strictly aseptic, technique. One series of tracheal grafts were preserved in Tyrode's solution by a method similar to that reported by Gross[11] for the preservation of blood vessels. A second group of tracheal grafts were preserved by rapid freezing in a bath of methyl alcohol and dry ice and kept at a temperature of 70° C. below zero. A third group of tracheal grafts were preserved in a 4 per cent solution of formaldehyde. A segment of cervical trachea containing three to six cartilage rings was excised, and the resulting defect bridged with a homologous tracheal graft. This graft was fixed in position with interrupted No. 40 cotton sutures. An attempt was made to use a graft which approximated as nearly as possible the diameter of the excised segment of trachea. The graft was usually one to two rings longer than the section of trachea removed. All animals in this and in the following studies received 400,000 units of penicillin daily for five days postoperatively. In this preliminary group of tracheal grafting experiments the results, shown in Table I, were the same whether the grafts were freshly obtained, frozen, or preserved in Tyrode's solution. Within a period of one to three weeks the grafted segment became narrowed to the point of complete obstruction.

From The Experimental Surgery Laboratories, University of California School of Medicine.

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TABLE I. TRACHEAL GRAFTING WITHOUT SUPPORTING TUBE

METHOD OF PRESERVATION	AGE OF GRAFT	LENGTH OF GRAFT	SURVIVAL TIME	RESULTS
Tyrode	1 week	4 rings	22 days	Expired
	2 weeks	4 rings	3 days	Obstructed*
	10 days	6 rings	24 days	Obstructed*
	5 days	4 rings	23 days	Obstructed*
	4 days	6 rings	14 days	Obstructed*
Fresh	–	6 rings	11 days	Obstructed*
Frozen	11 days	4 rings	11 days	Expired
	2 weeks	4 rings	3 days	Obstructed*

*Reoperated.

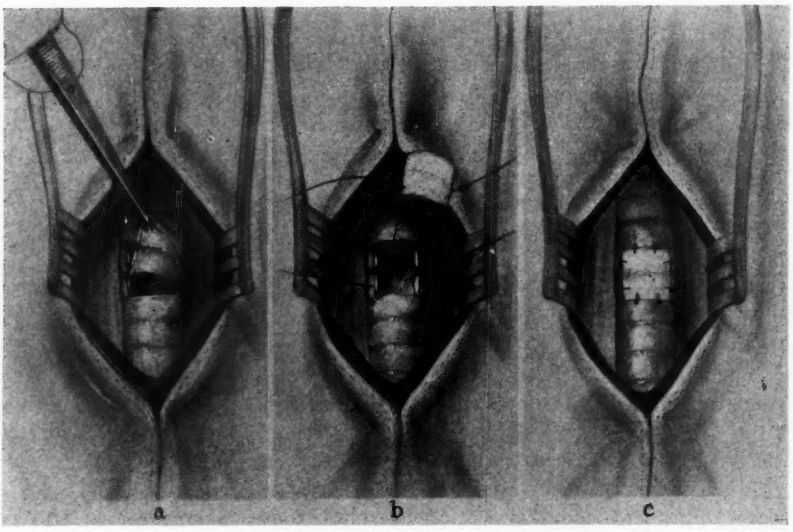

Fig. 1.—Creation of tracheal window and insertion of tracheal graft.

Microscopic examination of these specimens showed disintegration of the cartilage and replacement with fibrous tissue. The epithelial lining had disappeared, and the lumen of the transplanted graft was lined instead with chronic granulation tissue. The grafts preserved in formaldehyde were sloughed into the lumen of the trachea and were surrounded by a capsule of fibrous and granulation tissue. These grafts showed no evidence of being incorporated into the normal trachea.

From this group of experiments it appeared that, regardless of the method of preservation of the graft, postoperative stenosis developed in all instances in which no tracheal support was used.

In a second group of two animals a window was made in the anterior surface of the trachea. This defect involved two rings and one-third of the circumference of the trachea. A tracheal graft of comparable size and pre-

served in serum enriched Tyrode's solution was sutured into the area with interrupted No. 40 cotton (Fig. 1). No intratracheal supportive tubes were used in these dogs.

At the time of autopsy, four and one-half months after operation, these grafts were completely incorporated into the trachea (Fig. 2). The cartilage had survived, and the inner surface of the graft was covered by epithelium (Fig. 3).

Fig. 2.

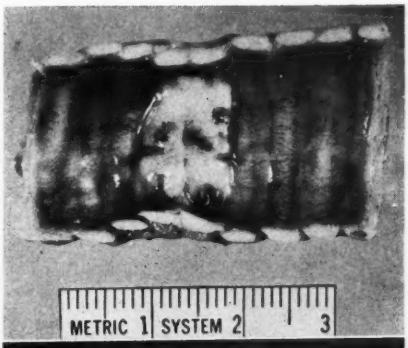

Fig. 3.

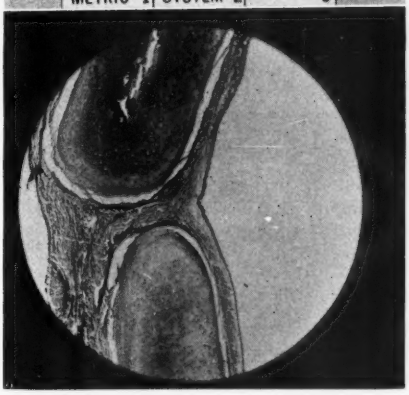

Fig. 2.—Gross appearance of tracheal window graft four and one-half months after operation.

Fig. 3.—Microscopic appearance of tracheal window graft four and one-half months after operation.

In a third group of experiments a method was developed in which an acrylic ("lucite") tube was used to splint the tracheal grafts inserted into the cervical and thoracic parts of the trachea.

The cervical portion of the trachea was exposed by a midline vertical incision and a segment of three to four rings of trachea excised. Into this defect a tracheal graft containing the specially designed acrylic tube was fixed in position with cotton sutures and No. 32 stainless steel wires, as indicated in

Figs. 4, 5, and 6. It was not necessary to use an intratracheal catheter during the grafting in the cervical trachea. These tracheal grafts were preserved in serum enriched Tyrode's solution for one to thirty days, and then implanted in seven dogs on eight occasions. In the first four animals the tube was fixed in position with No. 32 gauge, stainless steel wire, and became dislodged three to seven weeks later. A heavier, No. 24 gauge wire maintained the tubes in place in the last four successful cervical grafts. Three of these animals were alive and without respiratory symptoms after seven months of observation (see Table III).

Autopsy examination of the one animal sacrificed six months after tracheal grafting showed normal lung parenchyma. The acrylic tube remained securely in place (Figs. 7 and 8). The grafted segment showed cartilage remaining in its wall and complete regeneration of the lining by squamous epithelium (Fig. 9).

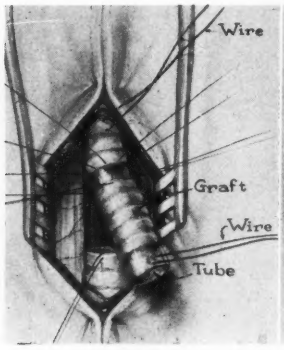

Fig. 4.

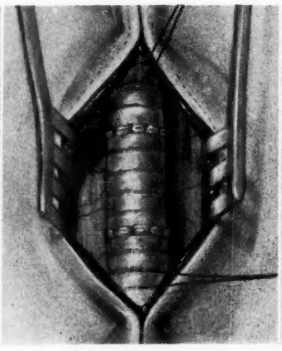

Fig. 5.

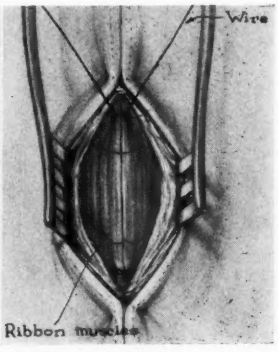

Fig. 6.

Fig. 4.—Insertion of graft containing acrylic tube.
Fig. 5.—Completion of suture lines.
Fig. 6.—Stainless steel wires passed through ribbon muscles and tied.

TABLE II. GRAFTING OF TRACHEAL WINDOWS WITH PRESERVED TRACHEAL GRAFTS WITHOUT SUPPORTIVE TUBES

METHOD OF PRESERVATION	AGE OF GRAFT	LENGTH OF GRAFT	SURVIVAL TIME	RESULTS
Serum enriched Tyrode's solution	2 days	1 by 1.5 cm.	4½ months	Sacrificed
	4 days	1 by 1.5 cm.	4½ months	Sacrificed

TABLE III. CERVICAL TRACHEAL GRAFTS USING ACRYLIC TUBE SUPPORT

AGE OF GRAFT	LENGTH OF GRAFT	SURVIVAL PERIOD	RESULTS
1 day	10 rings	20 days	Expired
1 week	8 rings	49 days	Obstructed*
12 days	6 rings	30 days	Expired
1 day	6 rings	49 days	Expired
1 day	6 rings	6 months	Sacrificed
1 mo.	6 rings	7 months	Living
2 days	6 rings	7 months	Living
15 days	6 rings	7 months	Living

*Reoperated.

TABLE IV. THORACIC TRACHEAL GRAFTS USING ACRYLIC TUBE SUPPORT

AGE OF GRAFT	LENGTH OF GRAFT	SURVIVAL PERIOD	RESULTS
4 days	5 rings	10½ months	Sacrificed
8 days	5 rings	10 months	Living
15 days	5 rings	8 months	Sacrificed
21 days	5 rings	10 months	Sacrificed
10 days	5 rings	10 months	Living
7 days	6 rings	8½ months	Living
Fresh	6 rings	5 months	Sacrificed
1 day	6 rings	5 months	Sacrificed
Fresh	6 rings	8 months	Living
14 days	6 rings	3½ months	Sacrificed

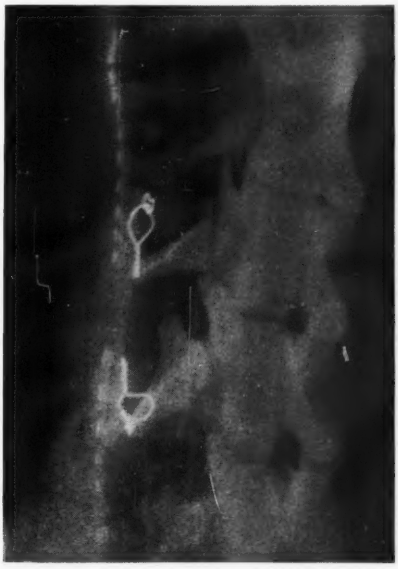

Fig. 7.—Roentgenogram of cervical trachea showing intratracheal acrylic tube in place.

In a fourth group of animals the thoracic trachea was exposed by an incision developed through the right fourth intercostal space. The right vagus nerve was injected with 2 c.c. of 4 per cent solution of procaine to obviate vagal reflexes. When the trachea was incised a sterile intratracheal catheter was placed into the distal end and secured by a suture of No. 40 cotton (Fig. 10). Controlled respirations were maintained through this catheter. A segment of the intrathoracic trachea 3 to 4 rings in length was excised, and a graft containing an acrylic tube was sutured in place in a manner similar to that described for the grafting of the cervical trachea. After the proximal suture line was secured, the intratracheal catheter was withdrawn. The distal sutures were then rapidly drawn up and tied, and respiratory exchange was maintained by means of an oral intratracheal catheter. The wire sutures were passed through the paravertebral musculature to prevent their erosion through the tracheal cartilage (Fig. 11). Air was withdrawn from the pleural

space by a rubber catheter, and the thorax closed without drainage. At the close of the procedure 5 c.c. of a solution containing 40,000 units of penicillin per cubic centimeter were instilled locally into the pleural space.

Fig. 8.

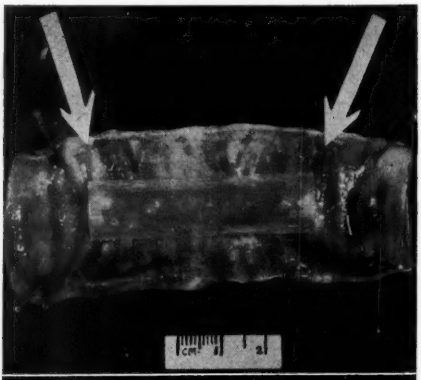

Fig. 9.

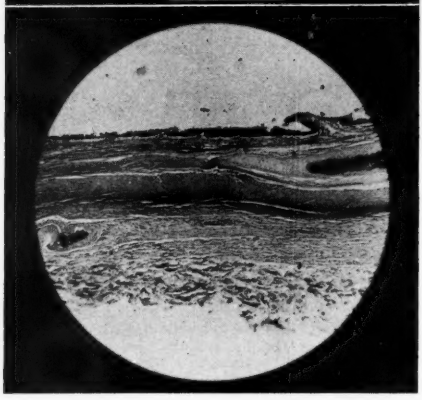

Fig. 8.—Gross specimen of grafted segment of trachea containing acrylic tube.
Fig. 9.—Microscopic section (×17.2) showing regenerated epithelial lining and cartilage remaining in cervical graft. Sacrificed six months after insertion of graft.

Ten animals had segments of thoracic trachea removed and replaced with tracheal grafts preserved in serum-enriched Tyrode's solution. These grafts were preserved from one to three weeks before they were used. The freshly obtained tracheal grafts were also used in this group of experiments. All of the dogs survived this operation, and have been observed for periods up to ten and one-half months postoperatively (See Table IV).

It was found that the tube could be removed readily by means of the bronchoscope, when the wires were broken or cut at a second-stage operation. The fine, No. 32 gauge wire was used in all of these animals.

In four of the six animals sacrificed at varying intervals, the wire had disrupted and the tube was dislodged. Autopsy examination revealed normal lung parenchyma. The graft was shortened and the lumen narrowed to about

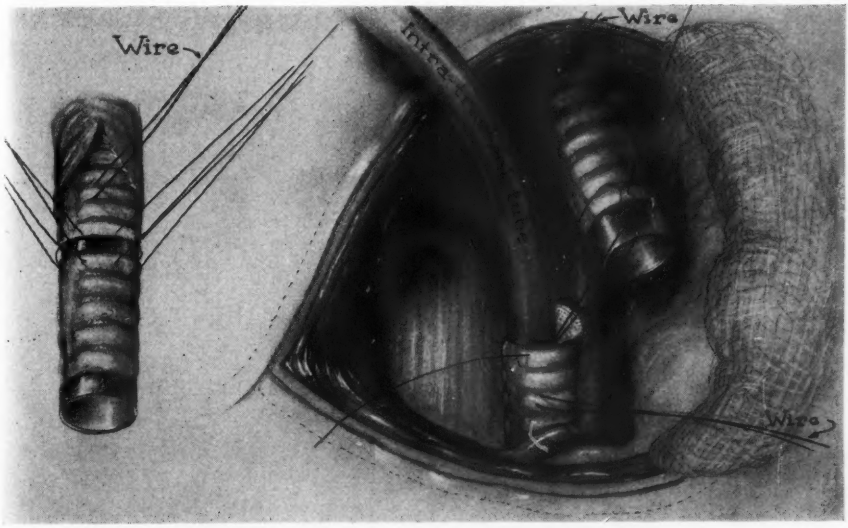

Fig. 10.—Sterile intratracheal catheter in place and graft being sutured into the trachea.

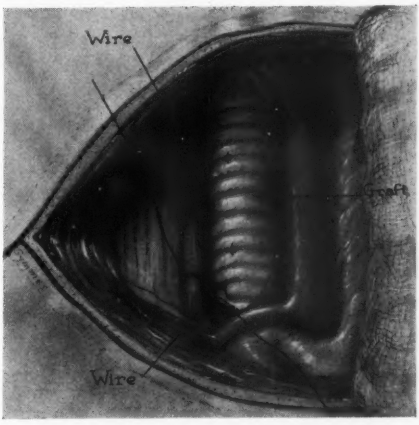

Fig. 11.—Completion of suture lines.

two-thirds of the normal diameter. One animal apparently had ejected the tube, as it was absent at autopsy. On microscopic examination of the grafted areas some chronic inflammatory reaction was observed; however, the grafts

TABLE V. PNEUMONECTOMY AND TRACHEAL GRAFT USING ACRYLIC TUBE

GRAFT AGE	SURVIVAL PERIOD	RESULTS
1 week	8 hours	Expired
3 days	6 hours	Expired
Fresh	1 week	Expired
5 days	3 months	Expired
4 days	7 months	Living

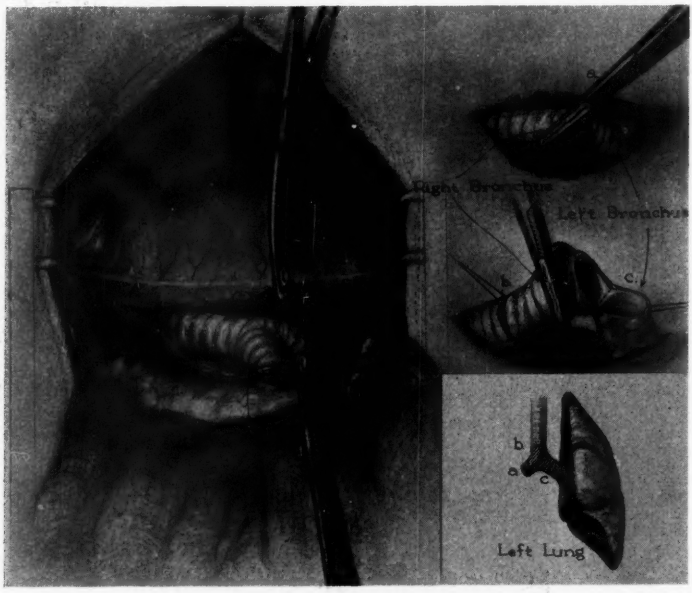

Fig. 12.—The right lung removed and the carina and a portion of the left main-stem bronchus to be removed.

were lined with squamous epithelium. Some cartilage remained in the area of the graft in all of these specimens.

In a fifth group consisting of five animals a right pneumonectomy was performed through an incision in the right fifth intercostal space. After removal of the right lung, the distal 3 rings of trachea, the carina, and first 2 rings of the main-stem bronchus were freed from the surrounding fascia and excised (Fig. 12). A free, homologous tracheal-carinal graft preserved in serum-enriched Tyrode's solution was then inserted into this defect by a technique similar to that already described for thoracic tracheal grafting (Fig. 13). The right main-stem bronchus on the graft had been closed with interrupted mattress sutures of No. 40 cotton and reinforcing continuous suture of No. 40 cotton. The acrylic tube used to splint this defect was slightly angulated and tapered to allow for the difference in size of the tracheal and bronchial stumps.

The first two animals in this group died six and eight hours postoperatively from leakage of the anastomosis and pneumothorax. One animal died one week postoperatively with disruption of the graft. One animal expired three months after operation, having developed a pneumonitis following a

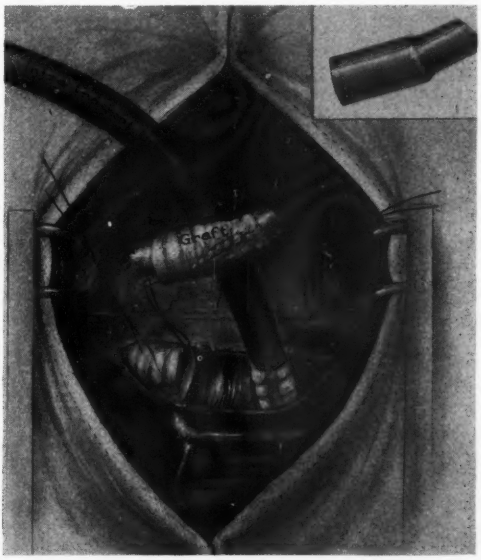

Fig. 13.—Tracheal carinal graft being inserted.

Fig. 14.

Fig. 15.

Fig. 14.—Specimen of left lung and trachea containing tracheal graft and acrylic tube.
Fig. 15.—Specimen of left lung and trachea containing tracheal graft and acrylic tube (specimen opened).

fight with another dog. Pathologic examination revealed the acrylic tube in place with well-defined cartilage remaining in the tracheal carinal graft (Figs. 14 and 15). There was pneumonitis and consolidation in the lower and middle lung fields. One animal remains living and apparently well seven months postoperatively (Table V).

SUMMARY

Preserved homologous tracheal window grafts have been successfully implanted into the trachea of two animals.

Complete homologous tracheal grafts have been implanted into the cervical and thoracic trachea in twenty-eight dogs with no operative mortality. In ten animals in which no means of internal support was used, the grafts became stenosed within one to three weeks after implantation. When cervical and thoracic homologous tracheal grafts were supported by an acrylic tube and held in position with stainless steel wire of appropriate size, the tubes remained in place for the duration of the experiment and caused no apparent difficulty. Cartilage has remained in these grafts for at least ten and one-half months, and the epithelial lining has been completely replaced by squamous epithelium during this period.

A method has been described for removing one lung, the distal trachea, carina, and a portion of the left main-stem bronchus of experimental animals, and bridging this defect with a tracheal graft and supporting acrylic tube.

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HODGKIN'S DISEASE OF THE LUNG WITH CAVITATION

Report of Three Cases

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HODGKIN'S disease is characterized by a marked involvement of lymphoid and reticulo-endothelial tissue. The location of the disease within the chest will therefore be determined by the distribution of these tissues, which are present in abundance in the interstitial tissue of the lung and the mediastinum.

The disease can originate in the lung itself, or the lung can be involved by direct invasion from affected glands in the mediastinum. The further spread of the process within the lung may follow the peribronchial or perivascular lymph vessels, and can result in peribronchitis or intrabronchial changes with granulations (Moolten[17]). Where the granulations and thickening of the bronchial wall are extensive, they may cause bronchostenosis, and the findings will be indistinguishable from a case of bronchiogenic carcinoma (Higginson[11]). Another form of spread within the lung is the more peripheral involvement of the alveolar wall, with the production of granulations followed by consolidation of lung segments or lobes resembling an ordinary pneumonia or pulmonary tuberculosis. A less common manifestation is the occurrence of well-circumscribed isolated nodules in the lung, giving a picture similar to secondaries in the lung. A miliary form has been described by Vieta and Craver.[3]

Central necrosis and the formation of cavities are not met with in Hodgkin's disease in other parts of the body, but cavitation does occasionally occur in the lungs, probably as a result of the special anatomy of the pulmonary tissue. When a cavity has been formed within the infiltration, pulmonary tuberculosis, lung abscess, or abscess in combination with a bronchiogenic carcinoma have to be considered in the differential diagnosis.

The symptoms caused by pulmonary Hodgkin's disease are more or less the same as those met with in the more common pulmonary diseases. They are fever, cough, night sweats, pain in the chest, loss of weight, and dyspnea. If a cavity is present the patient will probably cough up purulent sputum; hemoptysis is not common, but has been recorded. Changes may take place in the peripheral blood, and patients suffering from Hodgkin's disease may have a normal, high, or low, blood-cell count. The sedimentation rate is generally elevated. A positive diazo reaction in urine is suggestive, but not necessarily present. In about 10 per cent of the patients suffering from Hodgkin's disease one finds generalized pruritus which is a very troublesome complaint.

The prognosis in cases with pulmonary Hodgkin's disease is not as good as in patients afflicted with the same disease in other parts of the body. In the cases with pulmonary manifestations and cavitation reported in the literature, the survival from the time of the first symptom to death varies between two

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and nine years. The presence of constitutional symptoms is often met with in patients with pulmonary involvement, and is a bad prognostic sign.

During the last two years, three patients suffering from pulmonary Hodgkin's disease, with cavity formation, have been observed in our department.

CASE 1.—A. E., a woman, aged 30 years, previously had had no illness. In the autumn of 1947 she was vaccinated with B.C.G., but the Pirquet and Mantoux tests were still negative in May, 1948. In December, 1948, she became ill with fever, pain in the right side of the chest, and felt listless. She developed an unproductive cough and her B.S.R. was 110 mm. The Pirquet test was still negative, but the Mantoux test was found to be positive. A radio-

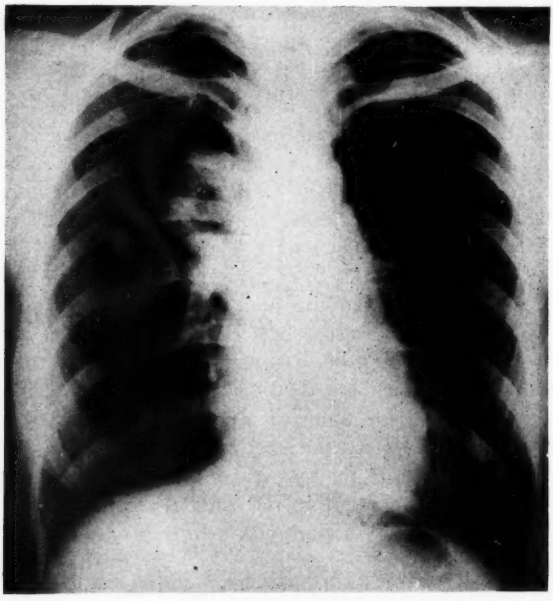

Fig. 1.—Anteroposterior radiograph showing a density in the right upper lobe with a cavity in Case 1.

graph of the chest showed an infiltration in the right upper lobe, and one month later a cavity had appeared in this opacity. In another hospital a diagnostic aspiration of the lung cavity was performed and purulent fluid obtained. The fluid was sterile, and on culture no growth of bacilli occurred. Because of the elevated temperature and her clinical appearance she was treated with systemic penicillin; this treatment was followed by a fall in the temperature and clinical improvement for a short time.

In the beginning of the year 1949 she became ill again with chills, elevated temperature, and this time coughed up a mouthful of blood-stained purulent sputum. After this she improved, and her condition was thought to be caused by a lung abscess.

She was admitted to the Surgical Department A in February, 1949. Her general condition was fair, she had moderate anemia, B.S.R. was 109 mm. The white blood cell count was 8,200, with 15 per cent lymphocytes. Bronchoscopy was negative. The radiographs of the chest showed a density with a large cavity in the anterior segment of the right upper lobe (Figs. 1 and 2).

Fig. 2.—Lateral tomograph showing the cavity in the anterior segment of the upper lobe in Case 1.

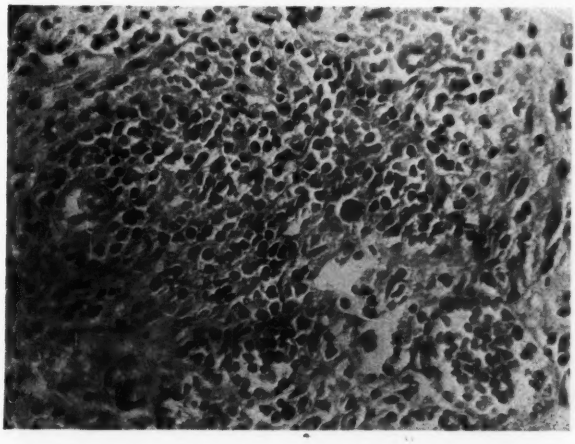

Fig. 3.—Photomicrograph of the involved lung in Case 1.

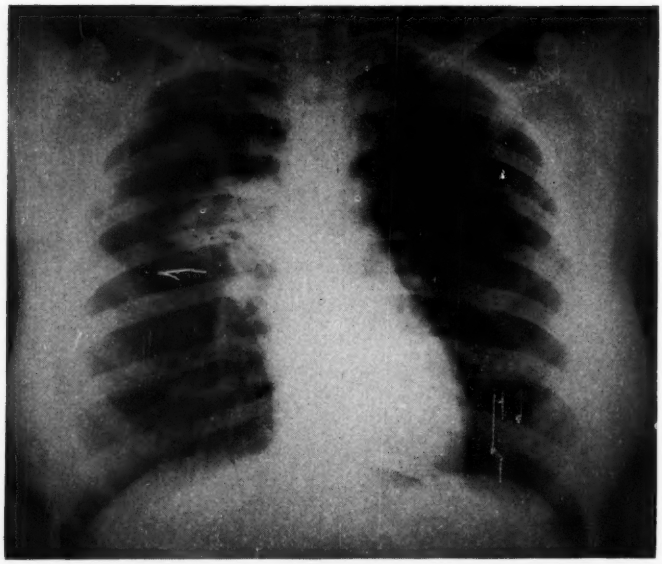

Fig. 4.—Anteroposterior radiograph showing a density in the right upper lobe with a cavity in Case 2.

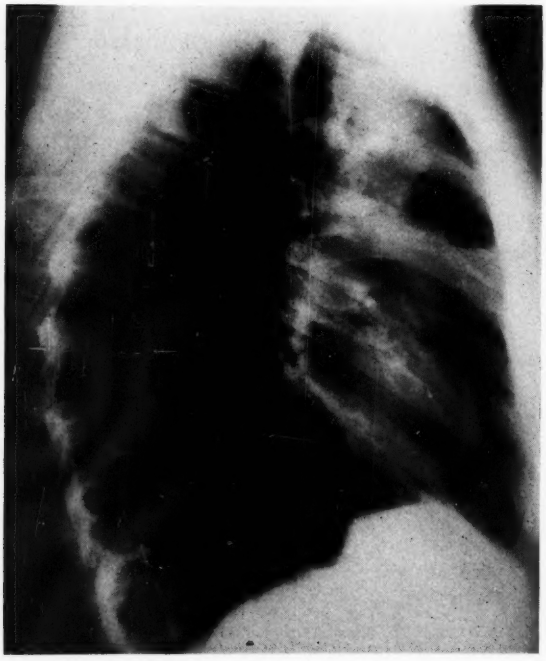

Fig. 5.—Lateral tomograph showing the cavity in the anterior segment of the right upper lobe in Case 2.

On March 2 a thoracotomy was performed on the right side. Firm adhesions were present between the chest wall and the anterior segment of the upper lobe, which was adherent to necrotic glands in the mediastinum. Along the internal mammary artery in the intercostal spaces, small fluctuating areas were found and were thought to be necrotic glands. A tuberculous process was considered the most likely diagnosis. The upper and middle lobe and the necrotic glands in the anterior mediastinum were removed.

The histologic examination of the lobes and the glands proved to be Hogkin's disease (Fig. 3).

The patient received postoperative radiotherapy, but later she developed a retrosternal fistula. She gradually lost ground, and died two years after the operation.

No post-mortem examination was obtained.

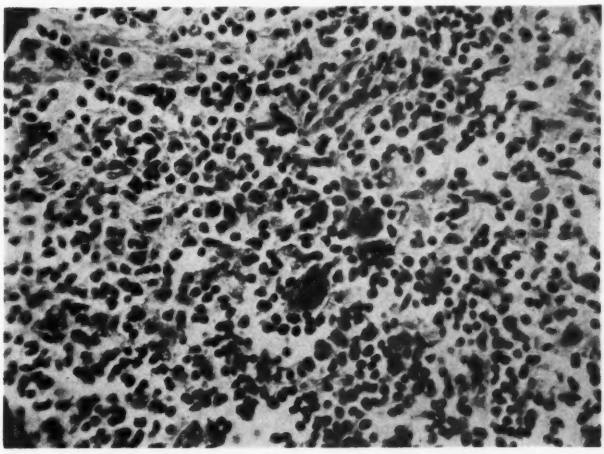

Fig. 6.—Photomicrograph of the involved lung in Case 2.

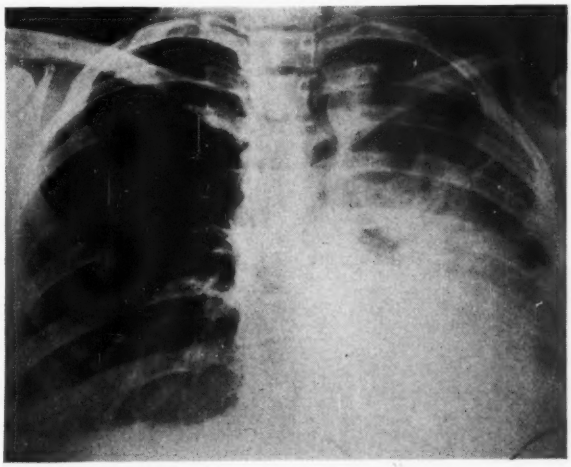

Fig. 7.—Anteroposterior radiograph showing infiltration of the opposite lung. The remaining lower lobe of the operated lung is clear.

CASE 2.—J. B., a woman, aged 21 years, who in 1948 had had jaundice of two weeks' duration. Otherwise she felt well, and there was no report of any previous illness. In the autumn of 1948 a routine mass radiograph revealed a density with cavitation in the anterior segment of the right upper lobe. She did not feel ill, but was admitted to a hospital for further investigation. The B.S.R. was 100 mm.

She was admitted to the Surgical Department A in February, 1949. Her general condition was good; there were no abnormal physical findings in her lungs. No glandular enlargement was palpated. She had a moderate anemia, B.S.R. was 66 mm., and the white blood cell count was 11,000, with 20 per cent lymphocytes. Bronchoscopy was negative. The radiographs of the chest showed a density in the anterior segment of the upper lobe with cavitation (Figs. 4 and 5).

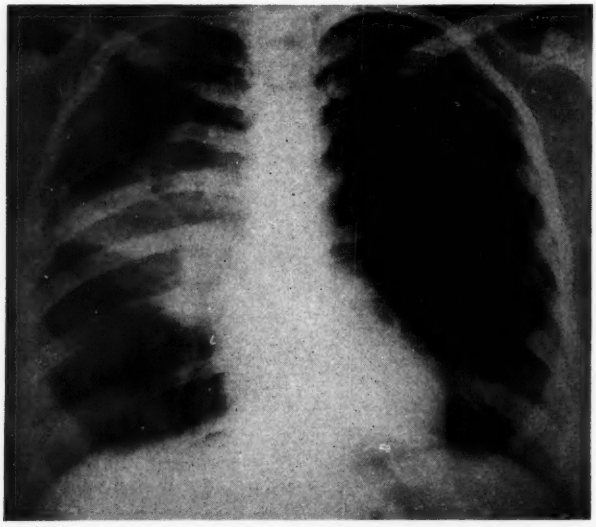

Fig. 8.—Anteroposterior radiograph showing a density in the right upper lobe with a cavity in Case 3.

On the diagnosis of lung abscess and the possibility of Hodgkin's disease, a thoracotomy was performed on March 4. A mass the size of a duck's egg was found in the anterior segment of the right upper lobe, which was adherent to the mediastinal pleura and the middle lobe. Some small glands along the upper lobe bronchus seemed to be involved. The upper and middle lobes were removed.

The histologic examination showed a polymorphous picture characteristic of Hodgkin's disease (Fig. 6).

She received postoperative radiotherapy to the mediastinum and to the operated side, but only five months later a shadow in the left hilum and one in the posterior part of the left lower lobe appeared. She was again treated with irradiation to the mediastinum and the left lung. In spite of this, the disease progressed on the left side, and her general condition deteriorated steadily. Two years later she had marked infiltration of the left lung (Fig. 7).

CASE 3.—I. H., a woman, aged 53 years, who previously had been healthy. A mass radiograph two years previously showed normal lungs and mediastinum. The Pirquet test was positive.

Fig. 9.—Lateral tomograph showing the cavity in the anterior segment of the upper lobe in Case 3.

Fig. 10.—Photograph showing involvement of the skin in Case 3.

In December, 1950, she developed an exanthema of the trunk and the extremities with a severe and troublesome pruritus.

In January her B.S.R. was 100, and she was advised to have a roentgenogram of her chest made. This showed a density in the anterior segment of the right upper lobe with a cavity. (Figs. 8 and 9.) She was admitted to the hospital for further investigation. Her general condition was good but she complained of severe itching and her exanthema showed many scratch marks (Fig. 10). The temperature was normal, and the B.S.R. was 57 mm. The white blood count was 26,000. There was a marked anemia (73 per cent). The diazo reaction was positive.

She was transferred to the Surgical Department A on March 15, 1951, with a diagnosis of Hodgkin's disease.

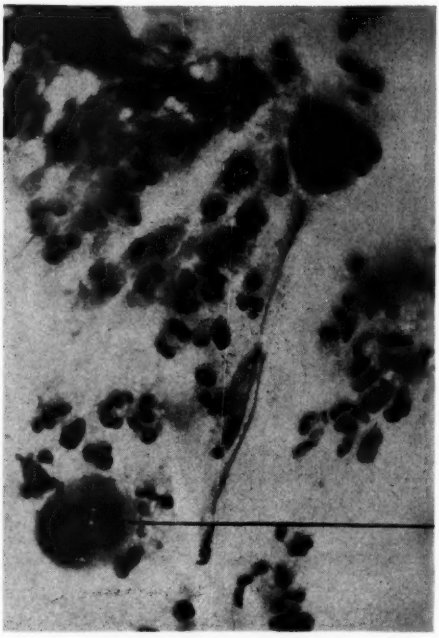

Fig. 11.—Photomicrograph of smear showing giant cells of the Reed-Sternberg type in Case 3.

Bronchoscopy showed some broadening of the carina, and from the right upper lobe bronchus reaccumulating purulent secretion was sucked out. A smear was examined and this showed giant cells very much like the Dorothy Reed-Sternberg cells (Fig. 11). A thoracotomy was performed on March 27, 1951, and a large mass was found in the anterior segment of the right upper lobe, and large glands in the mediastinum were densely adherent to the lung. The superior vena cava was embedded in the involved glands and firmly adherent. It was not considered possible to remove the glands radically, and only bits for section were taken.

The diagnosis was confirmed and proved to be Hodgkin's disease (Fig. 12). There was no evidence of tuberculosis. Postoperative irradiation resulted in some decrease in the pulmonary infiltration two months after operation.

DISCUSSION

The three reported cases were all women aged 20 to 53 years. The symptoms referable to the respiratory tract prior to admission were very slight.

They all had a high B.S.R.—100 or more mm. in one hour. The pulmonary lesions in all three cases were localized to the anterior segment of the upper lobe on the right side. They all had adhesions to the mediastinal pleura, and in all cases enlarged retrosternal glands were found. In none of the cases was general lymphadenopathy present.

In pulmonary Hodgkin's disease it will always be a problem where the primary site of the lesion is, if the disease has started in the lung or in the mediastinum. This will be of considerable importance in deciding the justification for surgical treatment.

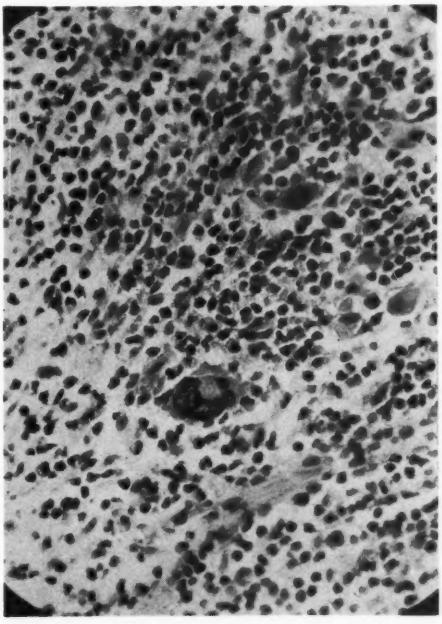

Fig. 12.—Photomicrograph of the involved lung in Case 3.

That the disease should have started in the lung and later extended to the glands in the mediastinum is not very likely, as the first group of lymph glands, situated along the larger bronchi, was involved in only one of our cases. The most likely sequence is that the disease in the lung has extended from involved glands in the mediastinum by direct extension through the pleura.

In the literature nine cases of Hodgkin's disease with cavitation in the lung have been recorded. The site of the process was the right lung except in one instance (Rubenfeld[19]). No clue, as to the primary site of the disease, was found in these cases.

A positive diazo reaction in the urine was suggestive of Hodgkin's disease in a patient with thoracic manifestations, as here described.

A bronchial smear examined for Reed-Sternberg cells can, as occurred in one of our cases, verify the diagnosis.

The treatment for pulmonary Hodgkin's disease will be as for Hodgkin's disease elsewhere: roentgen therapy, nitrogen mustard, or surgical removal of the localized focus.

If a cavity in the lung is present and it is possible to remove the involved glands in the mediastinum, a lobectomy or pneumonectomy followed by irradiation and possibly nitrogen mustard seems to be the most logical treatment.

If there are necrotic and secondarily infected glands in the mediastinum, as in Case 1, surgical treatment seems to be of little value, and in our patient only shortened the time of survival.

The prognosis with irradiation alone is in the first instant not too bad, and regression of infiltrations and disappearance of cavities have been reported.

In spite of the rarity of pulmonary Hodgkin's disease with cavitation, one ought to have it in mind in the differential diagnosis of the more common lesions in the lungs.

An effective histologic examination of the bronchial secretion may be of help in obtaining the correct diagnosis.

SUMMARY

Three cases of pulmonary Hodgkin's disease with cavitation are recorded. In all, the anterior segment of the right upper lobe was the site of the lesion. In all the cases the retrosternal mediastinal glands were involved. In one case the disease spread postoperatively to the other lung.

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BRONCHIAL ADENOMA

A Case Report

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MALIGNANT change in an adenoma of the bronchus was first reported by Zamora and Schuster[1] in 1937. Since then many articles have appeared with confirmatory evidence as to the potentially malignant status of the so-called bronchial adenomas, but there still remains some confusion in the literature regarding the exact histogenesis and nature of this neoplasm. However, in view of the possible malignant status of the tumor, it seems that the only feasible therapy is radical extirpation of the tumor and surrounding normal tissue. Nevertheless, local treatment is still advocated by some bronchoscopists. In order to accentuate the malignant possibilities of the bronchial adenomas, Doty[2] has recently re-emphasized that they are mixed tumors, as originally observed by Womack and Graham,[3] and suggested that they be called "mixed tumor adenomas." The following case is reported to illustrate the malignant potentialities of a bronchial adenoma, and to demonstrate that radical therapy may not always succeed.

CASE REPORT

C. H. H., a 26-year-old man, was first seen at the North Carolina Baptist Hospital on February 12, 1943. He was referred by his physician with the following note: "Onset of illness January 7, 1943, with high fever, nausea, vomiting, and pain in the left lower chest and left shoulder. He was started on one of the sulfonamides with marked improvement. However, in a few days the fever, nausea, and chest pain recurred, and he was admitted to the hospital. Left thoracentesis yielded 250 c.c. of blood tinged fluid, which was sterile to culture. A roentgenogram of the chest showed atelectasis of the left lower lobe with a shift of the mediastinum to the left. The patient improved after the thoracentesis, and was discharged from the hospital Feb. 5, 1943. He re-entered on February 9, with a temperature of 103° F., pain in the left lower chest, and cough productive of white frothy mucoid material. Chest roentgenogram still showed atelectasis of the left lower lobe." Additional history from the patient revealed that he had had an early morning cough, productive of small amounts of white sputum, and night sweats, for twelve months, with a 25-pound weight loss in this interval. Respiratory tract infections had been frequent every winter as far back as he could remember. Increasing shortness of breath, palpitation, and some clubbing of the fingers had been present for four or five years; this had been attributed to hay fever, which he had to a moderate degree. There was no history of exposure to or familial incidence of tuberculosis.

Examination: Temperature, 102.6° F., pulse rate, 104; respiratory rate, 24; blood pressure 115/78. The patient was a well-developed, acutely ill, young white man who was frequently stricken with paroxysms of coughing. The pharynx was moderately injected.

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The trachea deviated slightly to the left. The left lung below the fifth rib was dull to percussion, with absence of breath sounds and fremitus. The heart was shifted to the left. No other abnormalities were noted.

Laboratory Data: Urinalysis was negative. Hemoglobin 10 Gm., R.B.C. 4.8 million, W.B.C. 17,700, with 76 per cent polynuclearcytes. Sedimentation rate (Wintrobe, corrected) 49.5 mm. per hour. Kahn negative. Sputum negative for acid-fast organisms. A roentgenogram of the chest was reported as showing atelectasis of the left lower lobe. Bronchoscopy revealed a papillomatous growth at the orifice of the left lower lobe bronchus. A biopsy was taken and reported as follows: *Gross:* specimen consisted of a small fragment of tissue which measured approximately 1 cm. in diameter. *Microscopic:* Sections showed irregular islands of cells composed of epithelium of the basal type. Many cystic areas of degeneration were seen. The tissue for the most part was situated in a dense sclerotic fibrous tissue stroma; however, myxomatous areas were seen. *Diagnosis:* Basal-cell carcinoma of the bronchus. It was entirely possible that in this case an adenoma of the bronchus was being dealt with, and the material for study merely represented a basal portion of such a lesion.

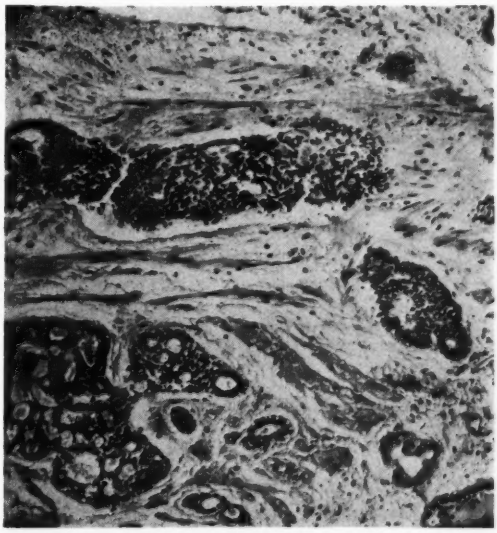

Fig. 1.—Photomicrograph of original biopsy specimen. (low power ×95), showing irregular epithelial glandular islands, with cystic degeneration.

Repeat bronchoscopy and biopsy were performed; the pathology report was as follows: *Gross:* specimen consisted of a small, rounded, dark, soft piece of tissue measuring 7 mm. in diameter. *Microscopic:* sections showed hemorrhagic surface beneath which were irregular epithelial cellular accumulations possessing degenerated centers. *Diagnosis:* The picture here was suggestive of adenoma of the bronchus. Since these tumors are the type which resembled so-called mixed tumors, it is possible that a basal element predominated in certain areas. The prognosis should be the same in either case. On Feb. 23, 1943, a left pneumonectomy was performed through the bed of the fourth rib anteriorly. The vessels and bronchus were ligated individually. As the papillomatous growth was cut through when the bronchus was first divided, another section was removed, thus taking practically all of the left main bronchus. The pathology report was as follows: *Gross:* specimen consisted of the left lung and a portion of the stem bronchus. Two large bronchi could be seen branching from the main bronchus, and one of the two bronchi was thickened about its margin. Serial sections

were taken through this entire thickened portion to try to demonstrate the origin of the primary tumor which has previously had a biopsy taken from it. Several enlarged lymph nodes were attached to the separate portion of bronchus and also about the hilum of the lung. Upon dissection of all the large bronchi and many of the smaller bronchi, they were found to be rather markedly dilated and filled with a thick mucoid yellowish purulent-appearing material. *Microscopic:* Sections through the one separate bronchus which was thickened showed a tumor which was of the same type previously described in the biopsies. Portions of the external surface of the tumor were covered by bronchial mucosa. The tumor also extended deeper into the bronchus and in some instances could be seen between the cartilage rings of the bronchus. The tumor was composed of small cells with small dark nuclei, and the cells were arranged about a central cystic area. Sections through the various lymph nodes showed a chronic lymphadenitis. *Diagnosis:* Adenoma of the bronchus, basal-cell type, and chronic lymphadenitis. This tumor showed no evidence of malignancy. The postoperative course was complicated by a low grade persistent fever, but this finally cleared and the patient was discharged twenty-nine days after operation.

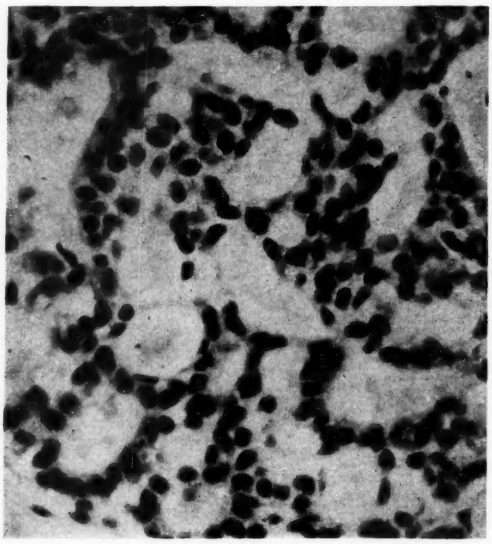

Fig. 2.—Photomicrograph (high power ×435) of a part of Fig. 1, showing cellular structure.

On Feb. 15, 1951, eight years after the pneumonectomy, the patient was readmitted to the hospital, this time complaining of hoarseness, which had been present intermittently for six to eight months. His health had otherwise been excellent; he had been able to work (watchmaker) without difficulty. Examination was negative except for slight hoarseness of the voice, and dullness over the left hemithorax. A roentgenogram of the chest showed a homogeneous density throughout the left hemithorax, with obliteration of the cardiac shadow. The right lung was clear. Laryngoscopy showed the left vocal cord to be immobile. Bronchoscopy revealed a small granular growth in the stump of the left main bronchus. A biopsy was reported as follows: *Gross:* Specimen consisted of a 2 mm. light brown irregular soft fragment of tissue. *Microscopic:* Sections through this tissue showed it to be composed of a loose connective tissue throughout which there were numerous basophilic cells that were fairly uniform in size, shape, and staining characteristics. These cells formed glandular structures which at times were incomplete. In all instances these cells appeared to be well differentiated. *Diag-*

nosis: Bronchial adenoma, recurrent. It was believed that he should have left thoracotomy with removal of the recurrent adenoma, which evidently involved the left recurrent laryngeal nerve. Under endotracheal anesthesia the fifth, sixth, and seventh ribs were removed, with the underlying parietal pleura, which was 4 cm. thick, extremely dense, and contained small deposits of calcium. The aorta, bronchial stump, and a portion of the pericardium were bound together in a dense mass. Attempts to separate the structures resulted in severe hemorrhage. It finally became necessary to abandon hope for removal of the bronchial stump. Bleeding was controlled by Gelfoam and hot packs. The chest wall was closed in layers without drainage. Four thousand cubic centimeters of whole blood were administered during the procedure, but nevertheless the patient went into profound shock soon after recovery from the anesthesia. Fifteen hundred cubic centimeters of whole blood given rapidly through an intravenous cannula alleviated the condition. The postoperative course was complicated by severe pain, and a sense of dullness, just below the incision. This was controlled by multiple intercostal nerve procaine blocks. He was discharged on the thirteenth postoperative day to be followed in the Out Patient Department. There had not been any change in his voice. It is anticipated that repeated bronchoscopic removals of the growth will be required.

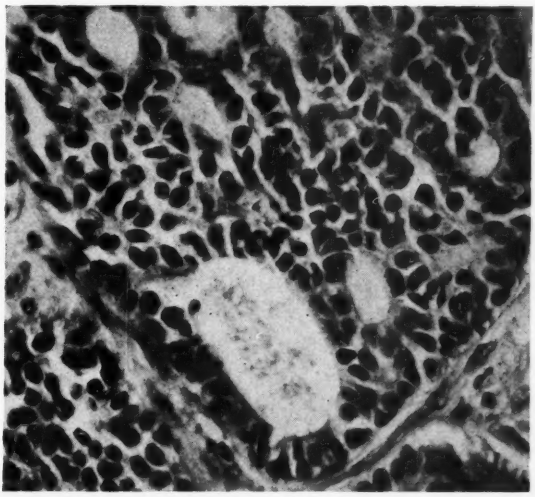

Fig. 3.—Photomicrograph of specimen removed eight years after specimen shown in Figs. 1 and 2. Note similarity of cells (×435).

The recurrence of the tumor was not anticipated. At the original operation the lymph nodes removed with the lung showed no involvement by the tumor. Also, serial sectioning of the bronchus revealed that the site of the second resection was well above the bounds of the tumor. The fact that a recurrence did occur indicates that either undetected local extension was present, or that the regional lymph nodes were invaded at the time of the original therapy. The former seems more feasible in view of the location of the recurrence.

This tumor was recognized as being of mixed origin, in that it showed at various times basal-cell cancer, myxomatous areas, and the typical bronchial adenoma structure; that it was thought to show "no evidence of malignancy"

was a misinterpretation. The long quiescent period (eight years) attests to a slow rate of growth, but does not detract from the malignant nature of the tumor.

SUMMARY

This is a case report of a patient with a bronchial adenoma that showed the characteristics of a mixed tumor, and subsequently recurred eight years after pneumonectomy. It appears that the appellation "mixed tumor adenoma" is more appropriate than adenoma, as applied to such neoplasms of the bronchus.

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CHONDROMATOUS HAMARTOMA OF THE LUNG

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INTRODUCTION

PRIOR to 1940 benign cartilaginous tumors of the lung, usually referred to as "chondromas" or "hamartomas," were considered rare and without clinical significance. Recent studies of surgically removed specimens, especially of round, so-called "coin" lesions, indicate that cartilaginous tumors are not uncommon. In fact, they have to be seriously considered in the differential diagnosis of asymptomatic, circumscribed pulmonary infiltrates discovered on routine chest roentgenography. Experience from a single institution may be cited as in indication of the increased frequency of detection of these tumors. In 1945, McDonald, Harrington, and Clagett[1] referred to three hamartomas resected at the Mayo Clinic. Five years later, Lemon and Good,[2] from the same clinic, described the radiographic features of no less than seventeen surgically removed specimens. Among thirty-three clinically silent solid pulmonary lesions removed surgically, Husfeldt and Carlsen[3] found five hamartomas as compared to only four primary carcinomas.

Recently, one of us (M. R.) removed three cartilaginous tumors of the type described as "chondromatous hamartoma." Even in this small group of cases certain features of the tumor were so striking that we were prompted to study the problem further. In addition to the three surgically removed tumors, twenty-eight similar growths found on post-mortem examination at Montefiore Hospital were studied, making a total of 31 cases.

CASE REPORTS

CASE 1.—S. K., a 54-year-old white man, developed pain in the right shoulder. In the course of a roentgen examination of the chest, a nodule was discovered in the right lung. A routine roentgenogram of the chest taken two years previously had been reported as "negative." Incidentally, the pain was found to be due to subdeltoid bursitis. There were no symptoms referable to the respiratory system. The chest roentgenogram revealed a well-defined, round density measuring about 1 cm. in diameter situated in the apical segment of the right lower lobe (Fig. 1*A*). The nodule was clearly defined on right lateral tomography (Fig. 1*B*).

The patient was admitted to Montefiore Hospital in June, 1948. Bronchoscopy was done on two occasions, but no endobronchial disease found. Smears and bronchial washings failed to reveal tumor cells. Because a definite diagnosis could not be established, exploratory thoracotomy was performed. A firm, round, nodular, yellow mass was found projecting from the lower lobe into the interlobar fissure. It was enucleated without difficulty. The patient made an uneventful recovery, and has remained well for three years.

The specimen consisted of a roughly rounded, sharply circumscribed, hard, grayish-white nodule, 1.5 cm. in diameter, with a whorled, coarsely lobulated surface. Microscopic examination revealed it to be composed predominantly of hyaline cartilage, arranged in a

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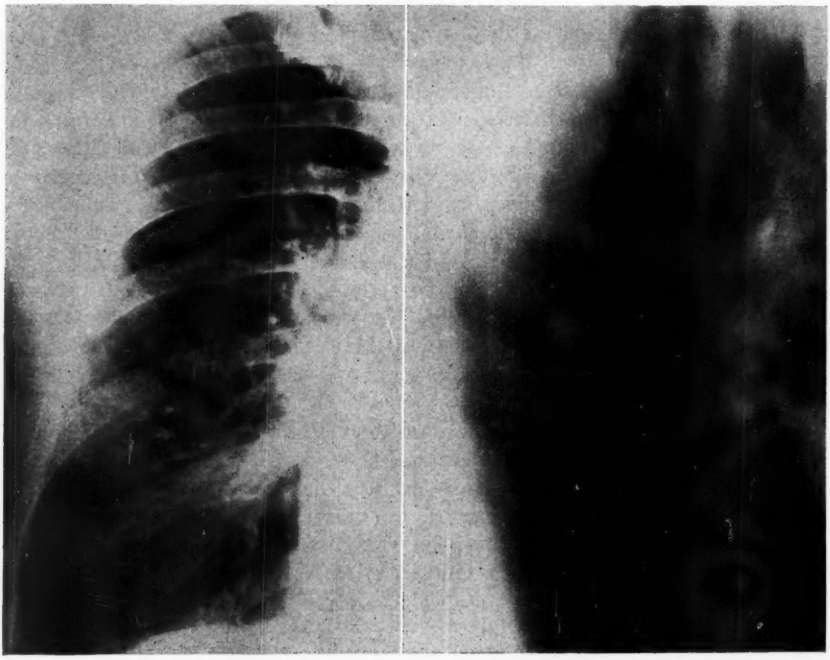
disorderly multilobulated pattern. The areas of cartilage were embedded in loose myxomatous connective tissue which filled the interstices and formed a thin peripheral rim completely surrounding the connected lobules of cartilage. Small bundles of smooth muscle, islands of adult fat tissue, and isolated glandular spaces were encountered in the stroma. The glands were lined by a single layer of epithelium which was cuboidal or columnar, and sometimes ciliated. In places this epithelium was continuous with similar cells, forming an incomplete layer around the surface of the specimen. Small papillae projected into some of the glandular spaces and from some points on the surface. No recognizable lung tissue was found.



A. *B.*

Fig. 1*A* and *B*.—(Case 1.) *A*, Preoperative chest roentgenogram of a 54-year-old man, showing a small, round mass in the right lung. *B*, Right lateral tomography. The tumor is located in the apex of the lower lobe.

Comment: The radiographic appearance of a circumscribed lesion in a previously normal lung suggested the diagnosis of a primary malignant tumor. The gross appearance of the lesion at operation indicated a benign tumor which could be removed by simple enucleation with preservation of the lobe. Very likely, the mass had been obscured by osseous structures in the x-ray film taken two years previously.

CASE 2.—F. P., a 52-year-old white woman, began to complain of shortness of breath in January, 1949, shortly after a round pulmonary mass was discovered on roentgen examination of the chest. It was soon apparent that the dyspnea was related to a nervous disposition rather than to the pulmonary disease. She was admitted to Lebanon Hospital in May, 1950. Bronchoscopic studies were negative. Radiographic examination of the chest revealed a well-circumscribed, rounded mass, 4 cm. in diameter, in the left lower lobe. In the left lateral

projection the mass appeared to be located in the interlobar fissure (Fig. 2). In view of the presence of calcification in the mass, a benign tumor of the lung was suspected. This assumption appeared substantiated by the fact that there had been no change in the size of the mass since its discovery fifteen months previously. At operation, a hard, yellow, nodular mass, 4 cm. in diameter, was found on the interlobar surface of the left lower lobe (Figs. 3 and 4). It protruded above the surface and was easily enucleated. The patient made an uneventful recovery.

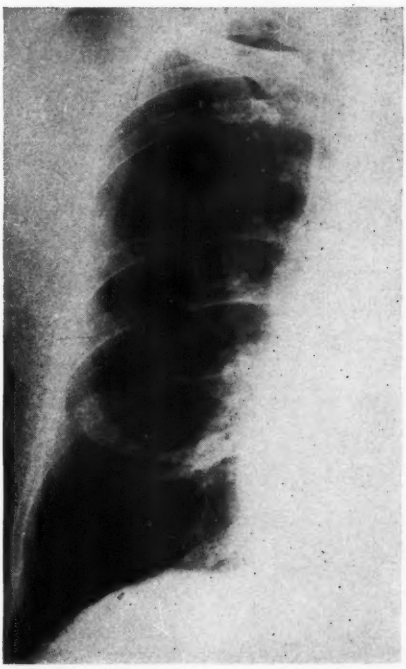
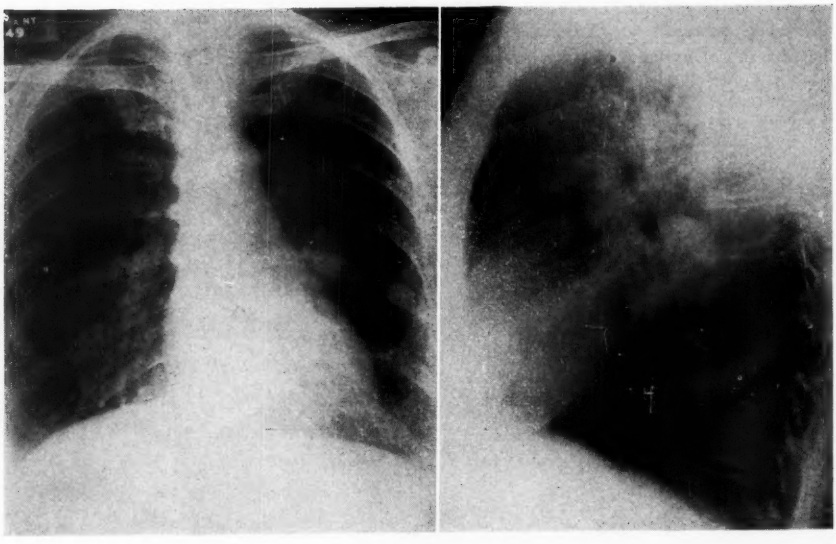


Fig. 1*C*.—Postoperative roentgenogram following excision of subpleural chondromatous hamartoma.

Microscopic examination of the mass revealed it to be nodular, of rubbery consistency and covered by a thin layer of pleura. Microscopically, it consisted of connected multiform islands of hyaline cartilage which were enmeshed in a mixture of loose myxomatous and dense collagenous fibrous tissue and fat. Bundles of smooth muscle and a few glandular spaces lined by cuboidal and low columnar epithelium were found at the margins and in the fibrous tissue between nodules of cartilage.

Comment: While the history and radiographic findings suggested a benign pulmonary neoplasm, a malignant lesion could not be excluded. The tumor was situated beneath the visceral pleura. The gross and microscopic appearance of this mass was similar to that in Case 1. The preoperative impression that the shortness of breath was not related to the lesion has been borne out by the fact that the patient still maintains she is short of breath.



A. *B.*

Fig. 2*A* and *B*.—(Case 2.) A 52-year-old white woman, complaining of dyspnea. *A*, Preoperative chest roentgenogram showing a circumscribed tumor in the left lung. *B*, Left lateral view. Mass is seen in the region of the oblique fissure.

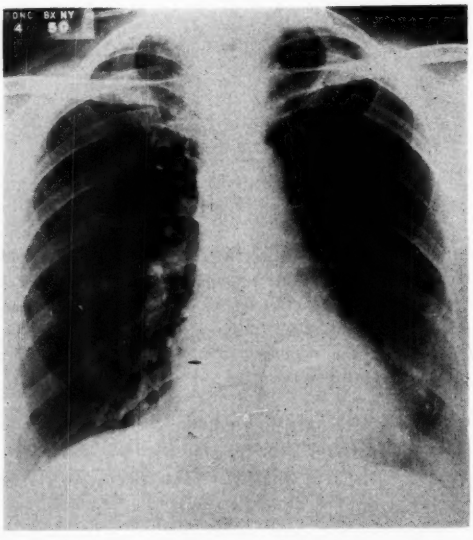


Fig. 2*C*.—Roentgenogram following operation. A hamartoma was found on the interlobar lobar aspect of the lower lobe.

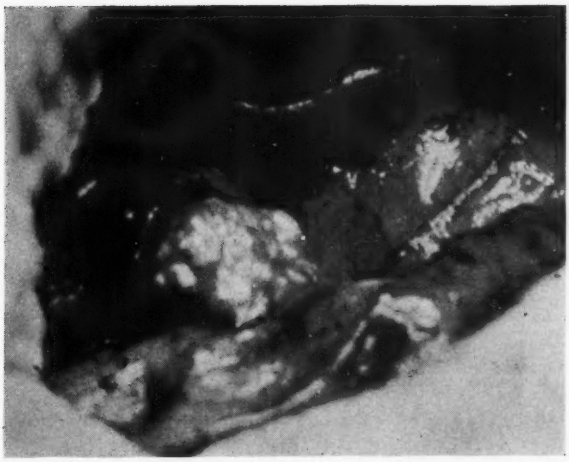


Fig. 3.—(Case 2.) Photograph at operation. A hard, nodular mass was found projecting from the interlobar aspect of the left lower lobe.

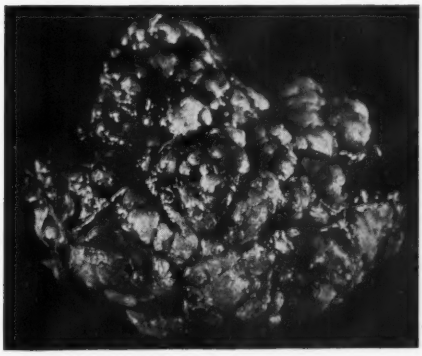


Fig. 4*A*.

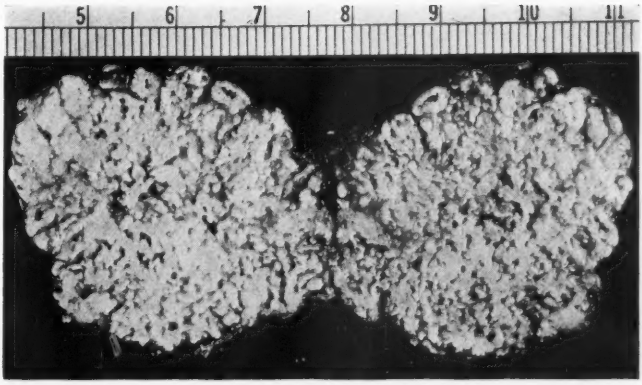


Fig. 4*B*.

Figs. 4*A* and *B*.—(Case 2.) *A*, Excised hamartoma from the left lower lobe. *B*, On cross section the mass is composed of numerous lobules with the consistency of cartilage.

CASE 3.—G. D., a 62-year-old, obese, white man, gave a history of bloodspitting of one week's duration. His past and family histories were negative for respiratory disease. He was admitted to the Thoracic Surgical Service of the Morrisania City Hospital in January, 1951.

Roentgenography of the chest revealed a rounded mass in the right lung, 4 cm. in diameter, just above the diaphragm. It was sharply circumscribed and mottled in appearance. Right lateral projection localized the mass to the middle lobe (Fig. 5). Bronchoscopy was negative. A preoperative diagnosis of hamartoma of the lung was made on the basis of the unique radiographic appearance of the mass, as well as on previous experience with such lesions.

At operation, a soft, circumscribed mass about the size of a plum could be palpated in the right middle lobe. It felt like a bean bag. Because of the history of hemoptysis, a right middle lobe lobectomy was performed. The patient made an uneventful recovery.

Fig. 5A.—(Case 3.) A 62-year-old white man with a history of hemoptysis. *A*, Anteroposterior roentgenogram of chest with a circumscribed, nodular mass above the diaphragm.

The specimen was a lobe of lung 13 by 7 by 4 cm. in size (Fig. 6). Its pleural surface was free of visible abnormalities. A compressible, sharply circumscribed, ovoid mass was felt beneath the pleura and measured 4 cm. in diameter. On section, it was separated from the surface by a thin rim of compressed lung tissue which was about 2 mm. in width at its narrowest point. The mass was coarsely lobulated, rubbery to soft in consistency, gray and translucent for the most part, but speckled with denser opaque gray-white foci. It was sharply circumscribed but not encapsulated, and was easily shelled out of its bed, leaving a smooth, deep depression traversed by compressed blood vessels and bronchioles. Relationship to a bronchus could not be demonstrated.

Microscopically, the sharp circumscription without encapsulation was confirmed (Fig. 7). The mass was composed of connected lobules of loose myxomatous, cellular, connective tissue, the free surfaces of which were covered by a continuous lining, varying from cuboidal to columnar and, in places, ciliated epithelium. In some areas a few mucous glands, adult adipose tissue, and small collections of lymphocytes were noted just beneath the surface epithelium. Small islands of poorly-formed hyaline cartilage were present centrally in only a minority of the lobules. None of the lobules revealed calcification or ossification.

Comment: The radiographic appearance of the tumor in this instance was more characteristic of a cartilaginous hamartoma of the lung than in the preceding cases. The mass found within the middle lobe was much softer in

Fig. 5*B*.

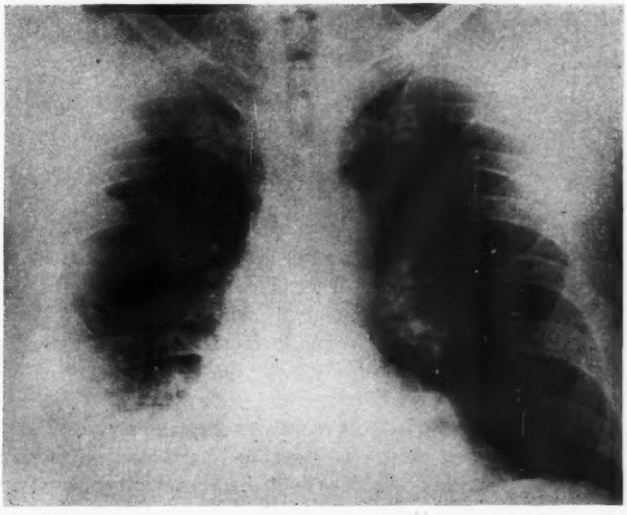


Fig. 5*C*.

Figs. 5*B* and *C*.—(Case 3.) *B*, Right lateral view. The tumor is located in the middle lobe. *C*, Postoperative roentgenogram following right middle lobe lobectomy.

consistency than the lesions in the previous two cases, due to the fact that it contained more myxomatous tissue and less hyaline cartilage. On dissecting the specimen, it was noted that the mass could be completely enucleated from the lobe. Hemoptysis has not recurred despite failure to demonstrate its source in the resected lobe.

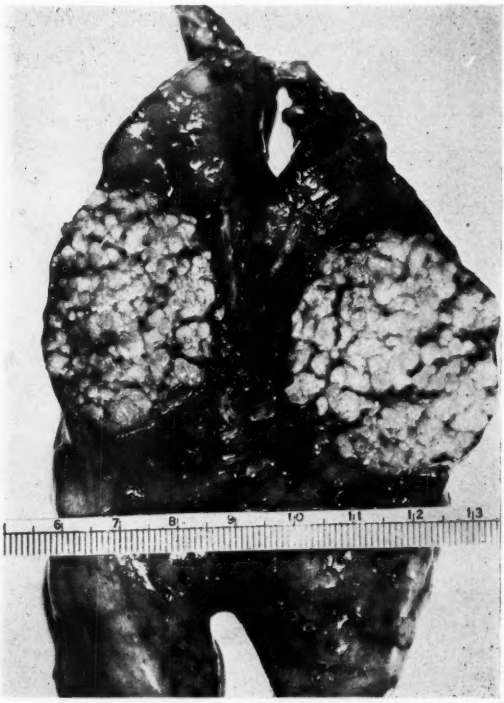


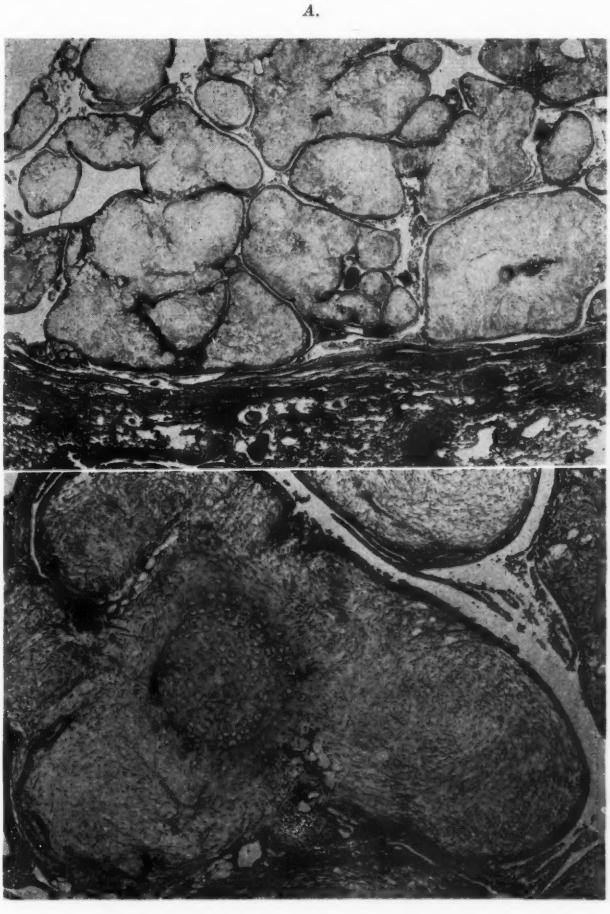
Fig. 6.—(Case 3.) Cross section of excised right middle lobe. Circumscribed tumor is situated below pleural surface consisting of numerous lobules.

ANALYSIS OF NECROPSY CASES

Solitary cartilage-containing tumors of the lung were found in twenty-eight of 8,800 post-mortem examinations performed at Montefiore Hospital between the years 1914 and 1949. This is an incidence of approximately one in 300 post-mortems. In each instance the tumor was an incidental finding, unsuspected during life in patients who died of various diseases. There were twenty-one males and seven females (Table I). A comparable sex ratio has been noted by others.

A review of the clinical records of the twenty-eight cases failed to reveal a single instance in which symptoms could be attributed to the cartilaginous tumors. Twelve of the twenty-eight patients had respiratory complaints related to either a primary or secondary pulmonary disease, including tuberculosis, primary or metastatic neoplasms, or cardiac diseases associated with congestive

failure. Even if symptoms due to the hamartomas had been present, they would have been very likely overshadowed by those due to the major illness. Roentgenograms of the chest were available in nine of these patients. The involve-



A.

B.

Fig. 7.—(Case 3.) *A*, Low-power photomicrograph of hamartoma in the right middle lobe. The lobulated tumor is surrounded by compressed lung (×15). *B*, High-power view showing composition of lobule of myxomatous connective tissue with central area of hyaline cartilage. The surface is covered by a continuous lining of cuboidal or columnar epithelium (×56).

ment of the lungs by other disease processes made it impossible to delineate the cartilaginous tumors with any degree of certainty, even when viewed in the light of the knowledge of the necrospy findings. Of the sixteen patients without primary or secondary involvement of the lungs, roentgenograms of the chest were available in seven. Two revealed shadows which had been over-

TABLE I. ANALYSIS OF TWENTY-EIGHT CHONDROMATOUS HAMARTOMAS FOUND AT AUTOPSY

CASE NO.	CHART	AGE	RACE	SEX	CAUSE OF DEATH	X-RAY FINDINGS	LOBE	SIZE	LOCATION IN LOBE
1	D. S. 8671	45	W	M	Pulm. tbc.	None available	R.U.L.	3 × 1.5 cm.	Midportion of lobe
2	B. L. 12536	61	W	F	Spinal cord tumor	Round lesion R.U.L.	R.U.L.	1 × 1 cm.	Subpleural
3	I. E. 32747	46	W	M	Chronic lymphatic leukemia	Negative	L.L.L.	5 mm.	Subpleural
4	N. M. 34953	80	W	M	Adenocarcinoma of stomach	No masses of pleural fluid	L.L.L.	1 × 1 cm.	Midportion of lobe
5	L. C. 15898	82	W	F	Heart failure	None available	L.L.L.	?	Subpleural
6	H. K. 16376	65	W	M	Carcinoma of lung	Multiple nodules	L.L.L.	?	Wall of bronchiole
7	W. K. 33704	71	W	M	Carcinoma of liver	Mass size of walnut	R.L.L.	2 × 2 cm.	Attached to medium sized bronchus
8	E. R. 35291	67	W	M	Heart failure	"Density in L.L.L."	L.L.L.	2 × 2 cm.	Subpleural
9	S. T. 27332	66	W	M	Adenocarcinoma of stomach	None available	L.L.L.	?	Subpleural
10	A. G. 25215R	47	W	M	Acromegaly	Negative	L.U.L.	?	1 cm. below pleura
11	M. N. 33523R	67	W	M	Adenocarcinoma of rectum	None available	L.U.L.	1.75 × 2 cm.	Midportion of lingula
12	M. M. 35364	72	W	M	Pulm. tbc.	Plum. tbc.	R.U.L.	2 × 2 cm.	Subpleural
13	I. N. 32633	58	W	M	Plasma cell myeloma	Multiple nodules	L.U.L.	Microscopic	Midportion of lobe

14	B. R. 39451	68	W	M	Carcinoma of bladder	None available	R.M.L.	1.5 × 1 cm.	Endobronchial
15	D. M. 43551	78	W	M	Arteriosclerosis	None available	L.L.L.	5 × 10 mm.	Subpleural
16	H. B. 44248R	63	W	M	Carcinoma of esophagus	Diffuse pleural involvement	L.U.L.	1 × 1 cm.	Midportion of lobe
17	E. S. 39962	56	W	M	Diabetes mellitus, arteriosclerosis	Negative	R.L.L.	4 mm.	Wall of small bronchus
18	E. S. 41614	54	W	F	Adenocarcinoma of uterus	Negative	R.L.L.	?	Subpleural
19	P. K. 41606	40	W	F	Adenocarcinoma of breast	Negative	R.U.L.	1 × 1.5 cm.	Subpleural
20	F. M. 39481	63	W	F	Carcinoma of tongue	Multiple metastases	L.L.L.	3 × 4 mm.	Midportion of lobe
21	J. B. 36228	62	W	M	Reticuloendothelial sarcoma	Numerous infiltrations	R.L.L.	8 mm.	Subpleural (diaphragmatic surface)
22	S. H. 37238	68	W	F	Carcinoma of breast	None available	R.U.L.	2 × 2 cm.	Subpleural
23	M. J. 34109	72	W	M	Adenocarcinoma of stomach	None available	R.L.L.	1.5 × 1.5 cm.	Midportion of lobe
24	G. S. 25344	55	W	F	Carcinoma of breast	Multiple metastases	R.U.L.	Microscopic	Parenchyma near pleura
25	J. H. 51667	63	W	M	Myelofibrosis, cerebral vasc. accident	None available	R.L.L.	Microscopic	Subpleural
26	S. L. 28163	53	W	M	Rheumatic heart dis.	None available	R.U.L.	?	Subpleural
27	J. O. 30727	39	W	M	Carcinoma of rectum	Calcified tubercles	L.L.L.	?	Wall of bronchiole
28	C. P. 47468	54	W	M	Carcinoma of prostate	None available	R.M.L.	?	Midportion of lobe

looked in the ante-mortem reading of the films. These corresponded in size and location to the tumors found at necropsy. The failure to demonstrate the tumors in the remaining cases can be ascribed to their small size, or obscuration or both.

TABLE II. ANATOMIC DISTRIBUTION OF 31 CHONDROMATOUS HAMARTOMAS OF THE LUNG

Lobar Distribution.—			
Right Lung:		*Left Lung:*	
Upper lobe	7	Upper lobe	3
Middle lobe	3	Lingula	1
Lower lobe	6	Lower lobe	11
Total	16	Total	15

Fig. 8.—Post-mortem specimen (Table I, Case 14) of an endobronchial hamartoma in a branch of the right middle lobe bronchus causing localized saccular dilatation of the bronchus and partial atelectasis of corresponding pulmonary segment.

The anatomic distribution of the growths in thirty-one cases is summarized in Table II. It is apparent that the majority were in the lower lobes and were about equally divided in the two lungs. Twenty-four were located peripherally. Of these, sixteen were immediately subpleural, usually projecting above the surface of the lung. Ten were somewhat deeper, being separated from the surface by a zone of compressed pulmonary parenchyma which varied in width from a few millimeters to a few centimeters. A relationship to a bronchus or large bronchiole, which could be interpreted as a true connection, was found in five cases. In four of these the tumor merged imperceptibly with the wall

of a large bronchiole which, however, was neither compressed nor distorted. In one case (Fig. 8) the mass formed an obstructing intraluminary polyp in a major branch of the middle lobe bronchus. It was 1.5 cm. in diameter and caused a localized saccular dilatation of the bronchus, with partial atelectasis of the corresponding pulmonary segment.

The majority of the tumors were small, varying from 1 to 2 cm. in greatest diameter. The smallest was 0.4 by 0.3 cm., the largest 3.0 by 1.5 cm. Their macroscopic appearance recorded by as many prosectors as there were tumors was monotonously alike, and furnished striking evidence that these tumors are of a similar nature. On palpation, they were rounded or ovoid, sharply cir-

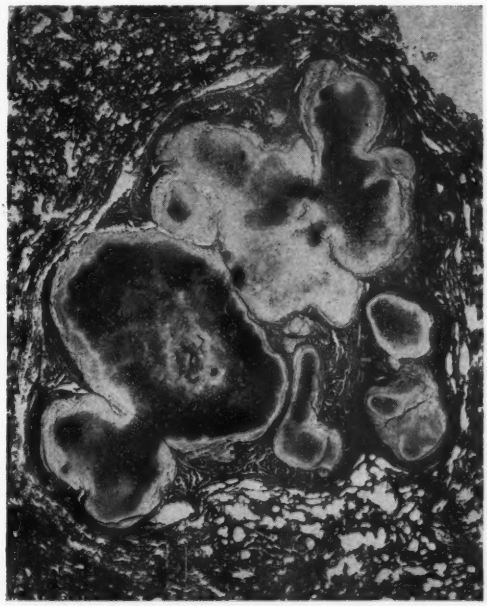


Fig. 9.—Low-power photomicrograph (×65) of a small hamartoma showing multiple, closely crowded, connected lobules, the most prominent component of which is a solid central island of cartilage. The tumor is not encapsulated but surrounded by compressed lung tissue (×15).

cumscribed, smooth, or coarsely lobulated. While most of the tumors felt hard and unyielding, some were rubbery and compressible. The cut surface resembled cartilage, the uniformity of which in some cases was interrupted by gritty, calcified, or ossified spots and streaks. With few exceptions, the masses were free of attachments to the adjacent parenchyma and could be easily enucleated, leaving a smooth defect. In some cases the macroscopic appearance was sufficiently characteristic to allow gross differentiation of the tumor from coexistent nodular cancerous metastases or tuberculous lesions elsewhere in the lung.

Microscopic preparations of each of the tumors were available and reexamined for the purpose of this study. Their histologic appearance was unique.

They were composed of mesodermal and epithelial elements in various proportions, but in a well-defined and uniform architectural pattern. They consisted of multiple, closely crowded, connected lobules, the most prominent component of which was a solid central island of cartilage (Fig. 9). In the majority, foci of calcification were present in the cartilage; less frequently isolated spicules of bone were encountered. The cartilaginous core was surrounded by a zone of fibrous connective tissue of variable width and structure. Usually, it was fibrillar and myxomatous in appearance but, at times, compact and collagenous.

Fig. 10.—High-power photomicrograph showing clefts between lobules with glandular spaces arranged in an irregular, papillary fashion and lined with cuboidal epithelium (×56).

A condensation of cellular elements in the transition zone, simulating perichondrium, was found in some cases. The free surfaces of individual lobules were covered by a layer of epithelium which varied from a low cuboidal type to tall and columnar, with or without cilia. This epithelium was indistinguishable from that lining normal subdivisions of the bronchial tree, and usually dipped into the underlying stroma to form distorted glands. Not infrequently, it protruded into the clefts between lobules, or formed glandular spaces in an irregular, blunt, papillary fashion (Fig. 10). Small sheets of adult adipose tissue were present just beneath the surface in the majority of cases. Strands of smooth muscle bundles and isolated lymphoid follicles were encountered less frequently. A definite capsule was not present. Adjacent alveolar septa, bronchioles, and small blood vessels were stretched and compressed. Histologic stigmas of malignancy were absent in all cases.

DISCUSSION

The vast majority of hamartomas of the lungs are found accidentally at post-mortem examination. In recent years, with the wider use of routine radiographic examinations of the chest and the attitude that asymptomatic solitary lesions of the lung, which otherwise defy diagnosis, warrant exploratory

thoracotomy, increasing numbers are being removed surgically. It is of interest that two of the three patients in whom this lesion was found at operation presented symptoms referable to the respiratory system. Yet, in both cases it is difficult to attribute the symptoms to the tumor. The difficulty in breathing in Case 2 has persisted following the removal of the mass. The middle lobe removed in Case 3 failed to reveal any source for bleeding which, however, has not recurred since the operation. It is very likely that the symptoms were not caused by the tumor in either instance.

Symptoms which can be attributed to hamartomas are absent, unless they produce bronchial obstruction or are large enough to compress adajacent structures. This feature can be correlated with the size and location of the majority of the tumors, both in our material and in the cases reported by others. Thus, we found a true connection with a bronchus or large bronchiole in only five cases. In four of these there was no compression. In one case the growth formed an obstructive endobronchial polyp (Fig. 8). Location within a bronchus is uncommon, this representing the fourteenth case of this type which has been reported.

Although on occasion the identity of the lesion may be suspected from the roentgen findings, only exploratory thoracotomy and pathologic examination of the tumor can substantiate the diagnosis. The radiographic findings illustrated in Case 3 led to a correct preoperative diagnosis. The roentgenogram accurately reflected the gross structure of the mass. Except in the unusual case in which the growth is located within a bronchus, additional diagnostic methods including bronchoscopy and cytologic study of material aspirated from the bronchus give little, if any, information because of the structure and peripheral location of the lesion. However, such tests are essential in order to rule out carcinoma or other diseases.

Hamartomas are usually ideally suited for surgical extirpation with minimal loss of functional lung tissue. Most hamartomas are peripherally located and easily accessible for enucleation through a small pleural incision. A few are centrally located and may require lobectomy, particularly if malignancy is suspected at operation. A rare form of massive hamartoma, almost replacing a lobe, has been encountered in a newborn infant at autopsy.[7] Objections to simple enucleation on the grounds of potential malignancy are theoretical on the basis of available data. With the possible exception of the case reported by Simon and Ballon,[9] there is no recorded instance of a true malignant neoplasm developing from a cartilaginous hamartoma of the lung. This statement is predicated on the opinion that cartilaginous hamartomas are biologically different from bronchial adenomas. The relationship of the latter to malignant neoplasm is well known. When located superificially, their appearance is sufficiently characteristic to allow recognition at operation. Where doubt exists, examination of frozen sections quickly establishes the diagnosis. No other tumor of the lung presents a similar histologic picture.

This study yields no original data to help elucidate the pathogenesis of the tumor of the lung under discussion; nor is it concerned, except incidentally, with problems of nomenclature and classification. Most of the cases in our

necropsy group were originally designated as chondromas. While their most striking component is cartilage, they invariably contain other mesodermal and epithelial elements. We were not able to find a single pure chondroma in the 8,800 necropsies reviewed. This might have been predicted from the accumulated experience of others, without necessarily denying that true chondromas exist in this location. It is significant, however, that on critical examination almost all reported extrabronchial "chondromas" of the lung are identical, consisting of a mixture of mesodermal elements in addition to cartilage. The current consensus of opinion is that these growths are tumorlike malformations resulting from an abnormal mixture of normal components of an organ. Some prefer the designations hamartochondroma or chondromatous hamartoma of the lung to differentiate these tumors from the vascular malformation of the liver to which the term was originally applied by Albrecht[10] and from the group of pulmonary tumors designated as adenomas.

CONCLUSIONS

1. Three cartilaginous hamartomas of the lung removed surgically, and twenty-eight found at post-mortem examination are reported.

2. Because of the increasing frequency with which this tumor is being encountered, the lesion must be considered in the differential diagnosis of all solitary, rounded pulmonary lesions.

3. A correct diagnosis may occasionally be made from the roentgen appearance of the lesion, but a definitive diagnosis can be made only by exploratory thoracotomy and examination of the mass.

4. Because of their unique microscopic appearance and their usually superficial location in the lung, most cartilaginous hamartomas can be readily identified in the operating room and removed by simple enucleation. Lack of familiarity with the characteristics of this lesion may result in needless sacrifice of lung tissue at operation.

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PULMONARY RESECTION AND UNDECYLENIC ACID IN SYSTEMIC BLASTOMYCOSIS

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IN 1894 Gilchrist[1] described the clinical picture of blastomycosis and identified the causative organism. He also suggested the use of potassium iodide in its therapy.

Numerous reviews of the literature give a complete clinical and laboratory picture of the disease.[1, 2] Two forms are recognized, the cutaneous and the systemic. The cutaneous type is characterized by single or multiple pyogenic granulomatous skin lesions. In the systemic type, single or multiple granulomatous lesions are present in the internal organs. About 50 per cent of all cases fall into each group.[1] The lungs are involved in over 90 per cent of the systemic group. The pulmonary focus is usually responsible for dissemination.[2] Cutaneous disease rarely results in dissemination.

The mortality rate of systemic blastomycosis is accepted as 90 per cent within three to five years after the onset of the disease.[1] Because methods of treatment have proved unsatisfactory, we have used previously unreported types of treatment in two patients. The first was a patient upon whom a pneumonectomy was done with the preoperative diagnosis of systemic blastomycosis which was localized to the right lung. A postoperative diagnosis was made in the second patient after the left lung had been removed as a palliative procedure with the mistaken diagnosis of carcinoma. Postoperatively he has been treated with undecylenic acid given orally.

Hoffman and associates[3] in 1939 showed the fungistatic effect of many fatty acids and their salts for certain nonpathogenic fungi. Their work resulted in the introduction of sodium and calcium propionate into the baking and dairy industry.

Keeney[4] was stimulated by Hoffman's work, and in 1943 studied the in vitro fungistatic and fungicidal effect of sodium propionate on common pathogens. At a pH of 5.5 complete fungistatic effect was obtained for blastomyces dermatitidis at a drug concentration of 0.0125 per cent. Results were poor at a pH of 7.4. Fungicidal activity was also demonstrated. Promising results were obtained for other pathogens including *Torula histolytica, Coccidioides immitis,* and *Histoplasma capsulatum.* In the same year Keeney and Broyles[5] reported good clinical results with sodium propionate on several varieties of superficial fungus infections.

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Keeney's[6] next work, reported a year later, had to do with the fungistatic and fungicidal activity in vitro of sodium valerate, sodium caproate, sodium caprylate, sodium caprate, and sodium undecylenate. Hoffman and coworkers[3] had reported that the fatty acids of these salts were most effective for nonpathogenic fungi at pH 7.4. These fatty acid salts were tested in vitro against fungi met in clinical practice as the common causes of the superficial and the deep mycotic infections. They showed that the salts of fatty acids acquire fungicidal activity as their chain is lengthened. The two highest chain salts, sodium caprate and sodium undecylenate, were shown to be the most promising fungicides. They were also the best fungistatic agents against the fungi that produce deep mycotic infections. Each produced maximum fungistatic activity at a concentration of 0.1 per cent (100 mg. per cent).

Thus we had evidence of the value of the fatty acids and their salts. Perlman's[7, 8] work reported in 1949 provided us with definite evidence that large amounts of undecylenic acid could be taken orally. Nineteen of his forty-one patients showed mild gastrointestinal disturbances when up to 19.8 Gm. of undecylenic acid were taken daily for long periods. He used it with controversial results in psoriasis and neurodermatitis. After treatment was started, we obtained further evidence of the drug's low toxicity from the work of Rattner.[9] He reviewed 1,100 cases of psoriasis treated with undecylenic acid. No figures were given as to dosage or form in which the drug was taken, but gastrointestinal upsets were said to have been frequent.

Before treatment was started, we determined the in vitro effect of undecylenic acid on cultures of *Blastomyces dermatitidis* from four patients (Table I). In all cases the organism failed to grow in a liquid broth mixture with a concentration of 10 mg. per cent of the drug.

Keeney and associates[6] had obtained complete inhibition of blastomycosis dermatitidis at 100 mg. per cent. This discrepancy in their and our results may be accounted for by three factors. They used the mold form of the organism in a solid medium medicated with sodium undecylenate. We used the yeastlike form of the organism in a liquid medium medicated with undecylenic acid. A liquid medium and the yeastlike or tissue form of the organism seemed more completely to simulate the conditions found in the systemic form of the disease. We believed that our collected evidence and results warranted trial of the drug.

TABLE I. SENSITIVITY OF BLASTOMYCES DERMATITIDIS TO UNDECYLENIC ACID

	STRAIN NUMBER			
	1 (MG. PER CENT)	2 (MG. PER CENT)	3 (MG. PER CENT)	4 (MG. PER CENT)
100 per cent inhibition	10	10	10	10
90 per cent inhibition			9	
75 per cent inhibition			8	
50 per cent inhibition	9		6	9
25 per cent inhibition		9	4	

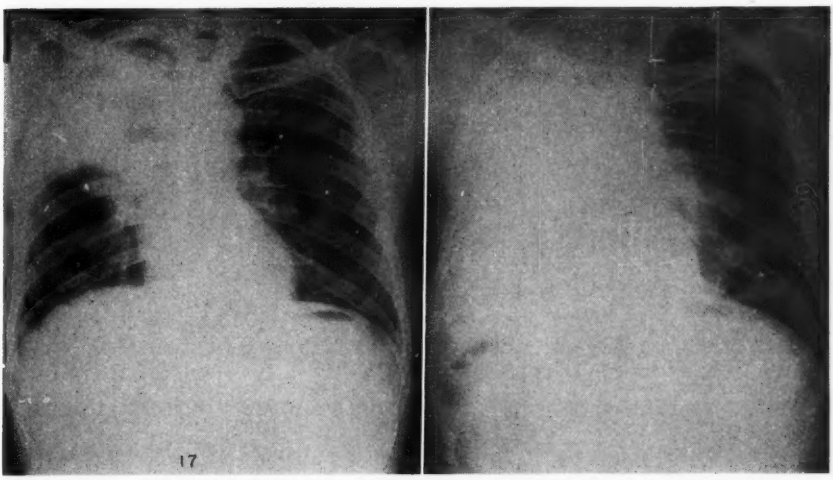
Sensitivity tests with undecylenic acid on four different strains of blastomyces dermatitidis. Tests done in tryptose phosphate broth (Difco pH 7.3) with the addition of 5 per cent horse serum. Incubated at 37° C. for seven days. Organisms tested in the yeastlike or tissue form.

Because of the previously unreported forms of therapy used, we are presenting two cases.

CASE REPORTS

CASE 1.—V. R., a 34-year-old Negro man, was admitted Dec. 17, 1949. Before World War II, he had done steel mill and construction work as a laborer. He served in the European and Southwest Pacific theaters. His past history was negative and previous health good.

The present illness began in 1945. On admission the original right chest pain, hoarseness, and streaking were still present. He also complained of fatigue, weakness, cough, fever, night sweats, anorexia, and 20 pounds in weight loss. With the exception of short periods of improvement of one or more symptoms, there had been gradual retrogression during this four-year period.



A. *B.*

Fig. 1.—(Case 1.) Preoperative (Jan. 5, 1950) and postoperative (April 19, 1950) films. *A*, Dense shadow in right upper lobe and superior segment of lower lobe. Pneumonectomy confirmed preoperative diagnosis of blastomycosis. *B*, Perihilar infiltration extending into lingula and left lower lobe. Autopsy confirmed clinical impression of progression of spread of blastomycosis in left lung.

Physical examination showed a chronically ill patient with temperature range of 100° to 103° F. daily. Examination of the right lung showed slight impairment of resonance, diminished breath sounds and posttussive râles (Fig. 1,*A*). The chest plate showed a pneumonic lesion in the right upper lobe.

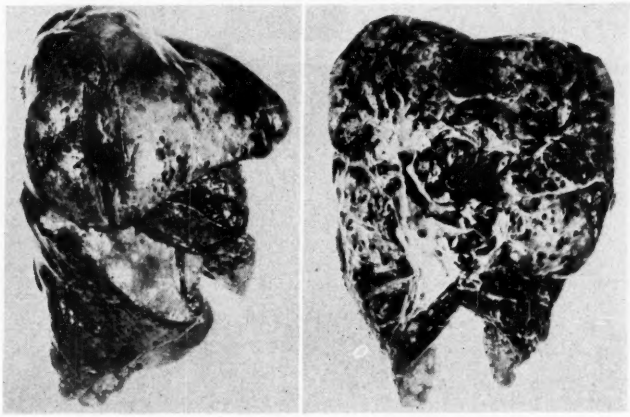
Admission blood studies showed a red count of 5,200,000, while the hematocrit was 46 and the hemoglobin 97 per cent. The total leukocyte count was 17,200, with 80 per cent polymorphonuclears, 18 per cent lymphocytes, 1 per cent monocytes, and 1 per cent eosinophils. During the rest of the preoperative course the eosinophil count did not exceed 3 per cent. The sedimentation rate (Wintrobe corrected) was 32 mm. per hour. Urinalysis showed a trace of albumin. The actual vital capacity was 2,600 c.c. compared to a normal for him of 4,550 cubic centimeters.

Smears and cultures were negative for tubercle bacilli, but positive for *Blastomyces dermatitidis*. Both the blastomycosis skin test and complement fixation test were negative. Electrocardiography was negative. Bronchoscopy showed a small amount of purulent material in the right upper lobe orifice.

After nineteen days of study, hospital care, and preparation, a right pneumonectomy was done on Jan. 6, 1950, in the face-down position, using cyclopropane anesthesia.

Figs. 2A and 2B.—In the gross specimen the upper lobe and part of the lower lobe were found to be firm in consistency. Cut sections showed pinkish-gray granulomatous areas with yellow foci. Numerous small cavities with firm walls were present.

Figs. 3A and 3B.—Microscopic examination disclosed numerous giant cells, epithelioid cells, and polymorphonuclear cells. Areas of pneumonia, pseudo-tubercles and micro-abscesses were interspersed. Numerous double contoured yeastlike organisms, about 20 microns, were identified in the lung.



A. *B.*

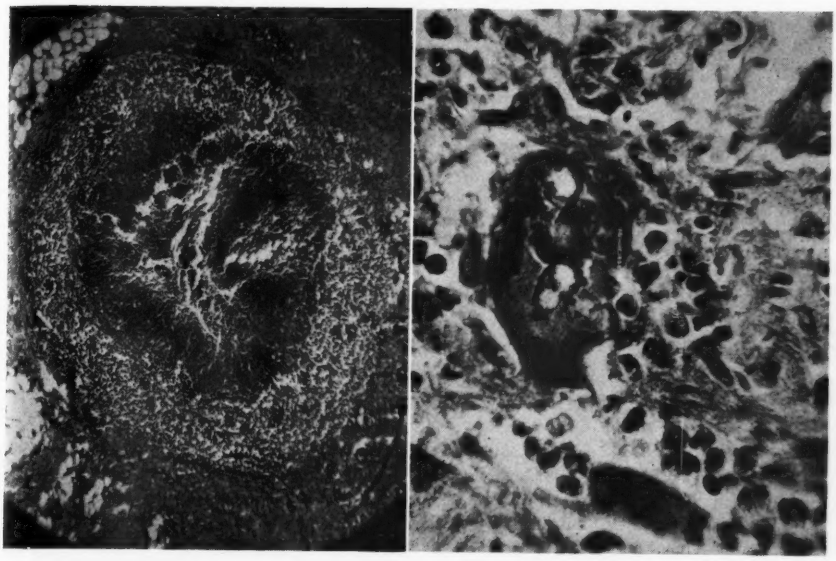
Fig. 2.—(Case 1.) Gross specimen of right lung (Jan. 4, 1951). *A*, Note consolidation of right upper lobe. *B*, Section of lobe shows numerous small cavities and confluent blastomycosis granulomas.

Figs. 4A, 4B, and 4C.—Culture on blood agar at 37° C. produced numerous small, heaped, wrinkled, waxy colonies after two weeks' incubation. Microscopic examination of the culture showed budding double contoured yeastlike organisms identical with those seen in the lung. Culture on Sabouraud's medium at room temperature produced a white cottony, aerial growth, typical of blastomyces dermatitidis.

A bronchogenic spread to the left lung was evident ten days after surgery. Since the skin test was negative desensitization with the blastomycosis vaccine was not done before potassium iodide therapy was started on Jan. 11, 1950. Treatment started with 30 drops daily. The patient was taking 300 drops (15 Gm.) by Feb. 28, 1950, when it was necessary to stop the treatment because of nausea. Small doses were again started but were stopped on April 17, 1950, when the dose had reached 420 drops daily. The patient's general condition was at this time much worse. The skin test had become weakly positive, and the complement-fixation test was positive to a 1 to 32 dilution. Desensitization was considered but subsequent skin tests were negative.

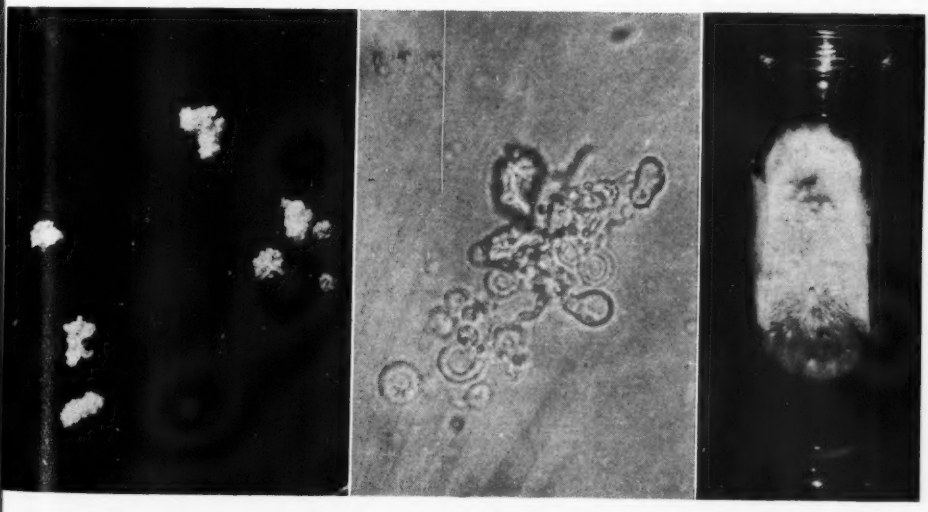
Fig. 1B.—Shortly before death, six months after the pneumonectomy, a film of the left lung showed progression of the disease. Exudative disease was seen throughout the central portion of the lung field. The costophrenic angle and the periphery remained comparatively clear.

Autopsy showed blastomyces dermatitidis granulomas in the left lung, the stump of the right bronchus, and empyema in the right pleural cavity. Organisms were also recovered from granulomas in the left kidney and heart.



A. *B.*

Fig. 3.—(Case 1) Photomicrographs of histologic preparations from right upper lobe. *A*, Low-power examination of blastomycosis tubercle. Tubercle indistinguishable from a tuberculosis process in this low-power magnification. *B*, High-power photograph (detail of Fig. 3*A* demonstrating double-contoured Blastomyces dermatitidis organisms in a giant cell.



A. *B.* *C.*

Fig. 4.—(Case 1) Smear and cultures, blastomyces dermatitidis. *A*, Blood agar at 37° C., two weeks. Note numerous small, heaped, wrinkled, waxy, cream-colored colonies. *B*, High-power photomicrograph, fresh potassium hydroxide preparation. Note budding, spherical, double-contoured, yeastlike organisms identical with those seen in the lung. *C*, Culture on Sabouraud's medium at room temperature. Note white cottony, aerial growth, typical of *Blastomyces dermatitidis*.

Comment.—This case of systemic North American blastomycosis presented a typical clinical course with characteristic signs, symptoms, and laboratory studies. The man's condition had gradually deteriorated during four years, with the disease apparently localized in the right lung. At the time of surgery the negative skin test and negative complement-fixation test suggested a doubtful prognosis.[10] Both tests became weakly positive after surgery. The development of the positive skin test indicates that the patient was developing some resistance. Iodide therapy did not help his general condition. We believe that if the bronchogenic spread had not occurred, life would have been considerably prolonged as a result of the pneumonectomy.

CASE 2.—A. P., a 40-year-old white man, was admitted Dec. 16, 1950, from the Veterans Administration Hospital, Fayetteville, N. C. He had entered there Oct. 24, 1950. His general health had been good up to the present illness. Two years before World War II service in 1944 he had worked in the Army Quartermaster Department at Goldsboro, N. C. Since the war he has continued as a watchmaker in Goldsboro. Military service was in the United States.

The present illness began at 4:30 A.M., Oct. 13, 1950, when he was awakened with pleuritic pain in the left anterior chest wall. He soon developed a cough productive of a small amount of gray-black sputum. Anorexia, weakness, and weight loss were progressive. Ten days after the onset he was admitted to the Fayetteville Hospital. Penicillin and aureomycin were given with no improvement. The temperature curve continued between 99 to 101° F. Smears and cultures were negative for tubercle bacilli.

On admission to Oteen, as a possible carcinoma of the left lung, all symptoms and signs continued. There had been a 20-pound weight loss since the onset. Examination of the right lung was negative. The left anterior chest wall showed limitation of motion. Dullness and decreased breath sounds were present above the third rib on the left. Blood pressure was 130/90, and pulse was 100.

Fig. 5A.—A chest plate of Jan. 3, 1951, showed atelectasis of the anterior segment of the left upper lobe with no evidence of cavitation. There had been no change since admission.

Laboratory findings showed a hypochromic normocytic anemia. The red count was 4,400,000, while the hematocrit was 44, and the hemoglobin 11.6 Gm. The total leukocyte count was 13,800, with 60 per cent polymorphonuclears, 32 per cent lymphocytes, and 8 per cent monocytes. In several other preoperative white counts eosinophils never exceeded 3 per cent. The sedimentation rate was 50 mm. per hour (Wintrobe corrected). Urinalysis showed a trace of albumin. The actual vital capacity was 2,500 c.c. compared with a normal for him of 4,600 cubic centimeters. Nine smears and one culture were negative for tuberculosis. Fungus smears and cultures were not made.

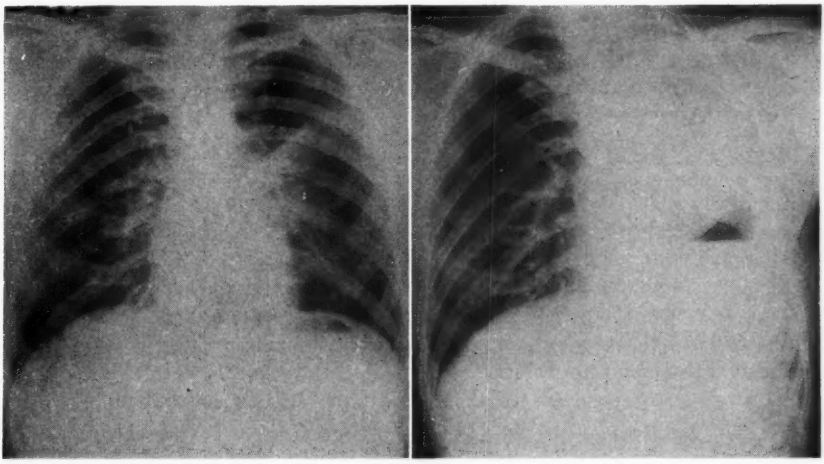
A small amount of pus in the left upper-lobe orifice was present at bronchoscopy. Bronchial washings were obtained and showed no evidence of malignant cells. Cytologic study was made on four sputum specimens. One was suggestive for carcinoma.

After nineteen days of study with eighteen days of streptomycin and six days of penicillin, there was no change in the clinical course. Exploratory thoracotomy was done Jan. 4, 1951, and confirmed the impression of atelectasis of the anterior segment of the left upper lobe. The segment contained a 4 cm. mass and with the lingula was densely bound to the mediastinum and anterior chest wall. The impression was that we were dealing with a carcinoma of the lung. It was necessary to remove a portion of the pericardium. The gross specimen showed atelectasis of the anterior segment with a mass of granulation tissue 4 cm. in diameter extending along and occluding the distal portion of the bronchus.

Microscopic examination showed a chronic granuloma characterized by agglomerations of epithelioid cells, giant cells, polymorphonuclears, and micro-abscesses. Yeastlike organisms were seen. Culture on blood agar and Sabouraud's media produced the typical colonies of *Blastomyces dermatitidis.*

The immediate postoperative course was stormy. Transient patchy atelectasis was present. Auricular fibrillation developed and was controlled with quinidine. There was marked dyspnea and mental confusion. The temperature curve was a septic type for thirty days. General condition was fair with little dyspnea after one month. Streptomycin, penicillin, and chloromycetin had been given for the first three postoperative weeks.

A blastomycosis skin test and complement-fixation test for blastomycosis were both negative two weeks after the resection. Fluid recovered from the left chest cavity Jan. 19, 1951, was positive for *Blastomyces dermatitidis* on culture. At the end of the first postoperative month the white count was 20,200, with 85 per cent neutrophils, 10 per cent lymphocytes, 4 per cent monocytes, and 1 per cent eosinophils.



A. *B.*

Fig. 5.—(Case 2.) Preoperative (Jan. 3, 1951) and postoperative (July 20, 1951) films. *A*, Dense shadow in anterior segment of left lung. No disease in right lung. Pneumonectomy (Jan. 4, 1951) showed atelectasis. The segment contained a 4 cm. mass of blastomycosis granulomatous tissue. *B*, The right lung is free of disease and the left thoracic cavity shows complete haziness with no evidence of disease.

Three weeks after surgery potassium iodide was started with nine drops daily. On March 7, 1951, when he was taking 54 drops daily, nausea developed and treatment was stopped. Desensitization had not been done since the skin test was negative. An emergency leave was given March 10, 1951, and he returned March 18, 1951, with serum jaundice. Because of the jaundice, potassium iodide was withheld. On April 21, 1951, he developed a papulopustular rash. This involved his face, scalp, gums, neck, ears, and both pectoral regions. The onset was associated with fever up to 101° F., which persisted for four days. Smears of the pustules were positive for *Blastomyces dermatitidis*.

On May 3, 1951, the patient was started on oral undecylenic acid capsules (0.44 Gm.) four, three times daily, for a total of 5.28 Gm. The white count at this time was 13,450, with 73 per cent neutrophils, 20 per cent lymphocytes, 4 per cent monocytes, and 3 per cent eosinophils. By the end of the first month the dose had been increased to 10.5 Gm. daily. The facial pain associated with the rash disappeared within ten days. Night sweats which had persisted soon ceased, appetite improved, and the patient began to gain weight.

After one month of treatment the skin lesions were confined to the forehead and shoulders. They now resembled small, healing furuncles. Smears and cultures were negative. The white count was 18,150 with 49 per cent neutrophils, 33 per cent lymphocytes, 9 per cent monocytes, and 9 per cent eosinophils. The sedimentation rate was 10 mm. per hour. The

blood level of undecylenic acid was determined by adding 1 part of the patient's serum to 5 parts of the media mentioned in Table I. This mixture resulted in 100 per cent inhibition to growth of the organism. Since it had been shown that the organism was completely inhibited by 10 mg. per cent of the drug, we now knew that the blood contained approximately 50 mg. per cent of undecylenic acid.

His condition was so good June 14, 1951, that he was given leave with instructions to take undecylenic acid at home. He returned from leave July 20. At this time a few very small pustules were present on the face. No organisms were found on biopsy, smear, or culture. He had no complaints. The weakness had disappeared completely and his appetite was very good. The blastomycosis skin test was now positive but the complement fixation test was still negative.

Fig. 5B.—A chest plate dated July 20 shows no evidence of disease. He was again instructed to take undecylenic acid at home.

When last seen Aug. 31, 1951, the hemoglobin was 17.3 Gm., the hematocrit 52, and the white count 9,600, with 58 per cent neutrophils, 35 per cent lymphocytes, 7 per cent monocytes, and no eosinophils. The sedimentation rate was 19. The chest plate was negative. A few furuncles which were present over the shoulders were negative to smear and culture for *Blastomyces dermatitidis.* He was allowed to return to work.

Comment.—This patient was admitted with infiltration in his left lung. We were dealing with an acute, rapidly debilitating lesion. Lack of a positive diagnosis required a thoracotomy with resection.

After a successful pneumonectomy which, however, did not eradicate the fungus, complement-fixation and skin tests were negative. The negative skin test indicated little resistance to the disease.[10] Four months after surgery he developed a dissemination of the organism. All recognizable manifestations of this tragic occurrence have disappeared under the influence of undecylenic acid. Eight months after surgery the skin test is positive and the complement fixation test is negative. The patient is now working with no complaints. We will continue the treatment.

DISCUSSION

In the past, surgery has not been used as a planned form of therapy for systemic blastomycosis with a unilateral pulmonary lesion. Collected figures show that less than 10 per cent of the systemic cases will live over five years. The survivors are usually in the group with a positive skin test and negative complement fixation test.

Our first patient with the negative skin test falls into the type of case with a poor prognosis. His case is, as far as we can determine, the first reported as treated by a planned pneumonectomy. Unfortunately, he did not survive.

The second patient, likewise with a negative skin test, fell into the 90 per cent of systemic cases not expected to survive. His diagnosis was made after excision of the primary lesion. Surgery did not prevent dissemination of disease, but it probably allowed development of some immunity, since his general condition improved in spite of postoperative jaundice.

Potassium iodide has been the only chemical available in the past. It has not prevented death in 90 per cent of the systemic cases. It has been of doubtful help in patients with a negative skin test. Schoenbach[11] recently

reported one patient with systemic blastomycosis treated with intravenous stilbamidine. The patient is still under observation but the author thinks he is cured. He suggests that the diamidines be tried in severe yeastlike infection.

Undecylenic acid has been shown to inhibit growth of *Blastomyces dermatitidis* in vitro at concentrations of 10 mg. per cent. Two months' treatment with undecylenic acid eliminated the cutaneous form of blastomycosis in our second patient. The skin test is now positive and his general condition is good eight months after surgery. We can demonstrate no evidence of systemic disease. The drug in combination with surgery seems to have prevented certain death.

We will use undecylenic acid in the treatment of new systemic blastomycosis patients. Careful clinical studies will be made. We plan to do in vitro sensitivity studies using several different fatty acids and their salts against the most common pathogenic fungi.

If a pulmonary lesion is present, which would be suitable for resection, and the diagnosis is made without exploratory thoracotomy, prolonged medication will be given. If surgery does eventually become necessary, we hope to have protection against dissemination. We believe the drug will prove of great value in patients such as the one we have treated when the diagnosis is made from the surgical specimen. We plan to use up to 20 Gm. of undecylenic acid daily over long periods. The patient herein reported has been on 10.5 Gm. of undecylenic acid daily for four months without symptoms due to the drug.

SUMMARY

1. Case histories of two patients with systemic blastomycosis have been presented. In each case the disease appeared localized to one lung. Each case was treated by pneumonectomy. We are not aware of similar case reports.

2. The first patient treated by planned pneumonectomy died six months after surgery. Iodide therapy seemed to have little effect on the spread in his left lung.

3. The diagnosis in the second patient was made after the lesion had been removed by pneumonectomy. A late spread occurred in spite of iodide therapy.

4. Disease in the second patient has either been controlled or cured by oral undecylenic acid.

5. We find no evidence that any of the fatty acids or their salts have been used to treat the deep mycotic infections.

We are indebted to Mr. Carl J. Hogue of the hospital laboratory section for his work with the fungus studies.

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THE OPEN CLOSURE OF THE BRONCHUS AND THE RESECTION OF THE CARINA AND OF THE TRACHEAL WALL

VIKING OLOV BJÖRK, M.D., ERIC CARLENS, M.D., AND CLARENCE CRAFOORD, M.D.
STOCKHOLM, SWEDEN

THE double lumen catheter constructed by Carlens for bronchospirometry and for one lung anesthesia has facilitated certain technical steps in lung resections to such a degree that it is now in daily use in our clinic.

The catheter* is made of rubber in two sizes. The lumen of each side corresponds to a circular area with a diameter of 7 mm. in the catheter for men and 6 mm. in the one for women. The total outer diameters are 13 and 11 mm., respectively.

The tube is introduced under topical anesthesia without the aid of fluoroscopy or bronchoscopy. Under mirror guidance it is introduced over a curved metal stylet. The rubber hook is tied down to the catheter with a moistened silk thread until the tube with a slight rotating movement has been passed through the larynx, when the slipknot is untied. The catheter is gently pushed downwards and turns automatically to the left when the curved stylet is withdrawn. During the introduction it exerts a slight pressure on the left tracheal wall and therefore enters the left main bronchus. It is then easy to feel when the hook is engaged by the carina. A slight pressure downwards is then exerted on the catheter when the cuffs are inflated. Then anesthesia and suction can be applied to each lung separately. The hook and the two rubber cuffs will maintain the catheter in correct position. It is not necessary nor advisable to have a higher pressure in the cuffs than enough to get an air-tight closure of the bronchus and the trachea. This is easily controlled when the artificial respiration is started.

It is also possible, either in general or in local anesthesia, to introduce the catheter over a straight metal stylet through a laryngoscope and remove the stylet and the silk thread as soon as the hook has passed the larynx. Many anesthetists prefer that technique, but in patients with a short neck and big teeth it may be of value to be familiar with the former procedure as well.

The experience from more than 300 resections has shown the main advantages of the flexible double lumen catheter for one lung anesthesia to be:

1. The open closure of the bronchus facilitating the resection of the carina and of the tracheal wall.

2. Prevention of transbronchial spread in wet cases and in tuberculosis making the "face-down" position unnecessary. Continuous suction can be applied to the bronchus draining the diseased area.

3. The lung can be deflated to provide more operating space when it is separated from the chest wall (see Fig. 2) and it can be inflated when lobar and intersegmental planes are developed (see Fig. 3).

Received for publication Oct. 8, 1951.

*The catheter described in this paper is obtainable from A. B. Stille-Werner, Stockholm 1, Sweden.

While points 2 and 3 have been described in an earlier paper, the advantage of the open closure will be discussed in this communication.

One lung anesthesia makes it possible to cut through the bronchus whenever this is suitable during the resection and to leave it open until it is convenient to close it. During the time the bronchus is left open the anesthetist leaves a small plastic catheter for continuous suction close to the cut edges of the bronchus to collect blood that may enter it.

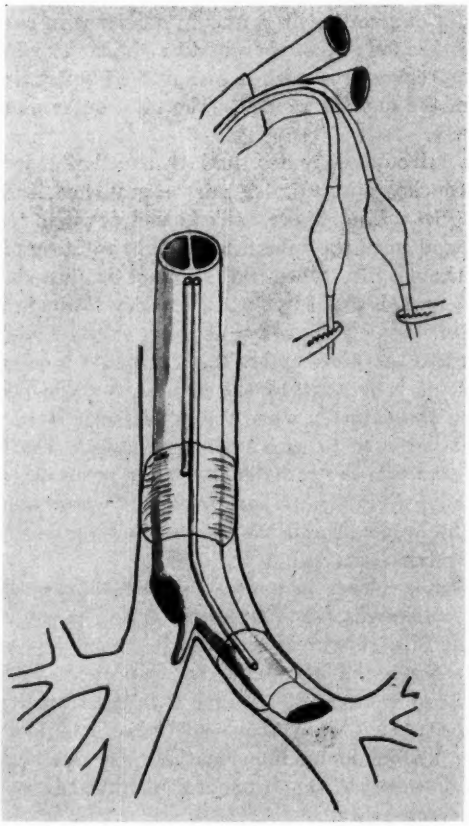

Fig. 1.—Diagram of the double lumen catheter in position. Notice the small rubber hook that is automatically engaged by the carina.

By this method it is not necessary to apply a clamp on the proximal part of the bronchus. If such a clamp is applied too firmly, it may injure the bronchial wall causing an impaired healing.

It may be possible to avoid the central bronchial clamp by other techniques, but the great advantage with one lung anesthesia is that there is no hurry in closing the bronchus. The bronchial tree can be inspected, bronchial

anomalies may be detected and the correct interpretation of the bronchial anatomy may be confirmed in segmental resections. Bronchotomies and local excisions of tumors from the bronchial or tracheal wall have been much facilitated, see Case 3, Fig. 9. Through the open bronchus aspiration with a small rubber catheter may easily be carried out.

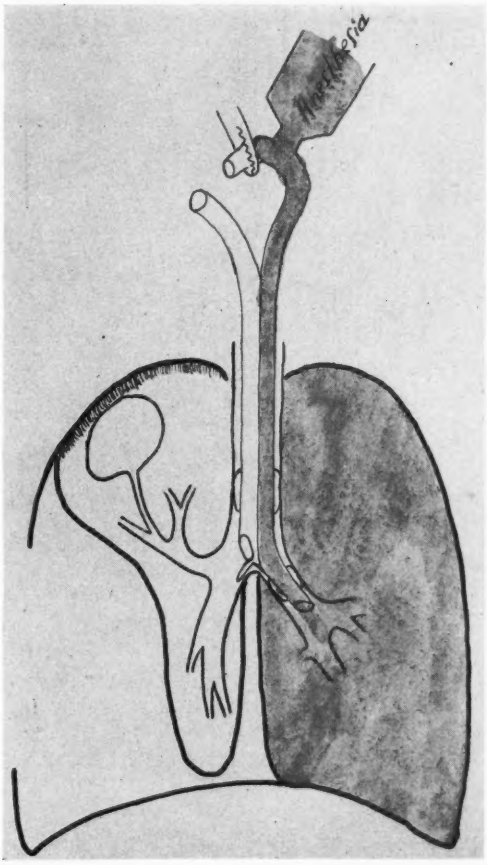

Fig. 2.—The lung can be deflated to provide more operating space when it is separated from the chest wall. Continuous suction is applied to the diseased lung and anesthesia to the healthy one.

I. Bronchial Closure by Invagination.—In pneumonectomies for tuberculosis without bronchial stenosis, the invagination technique according to Crafoord is preferred. The only danger of this technique is an obstruction of the proximal bronchus by the invaginated part. This may be avoided by a more exact estimation of the distance to the carina through the open bronchus. The invagination technique may also be performed in bilobectomies, but not

in lobectomies or segmental resections when the bronchial stump is too short and a simple closure is preferred. Furthermore, there is no need for the use of this technique in cases with partial resections, where lung tissue is left behind covering the bronchial suture.

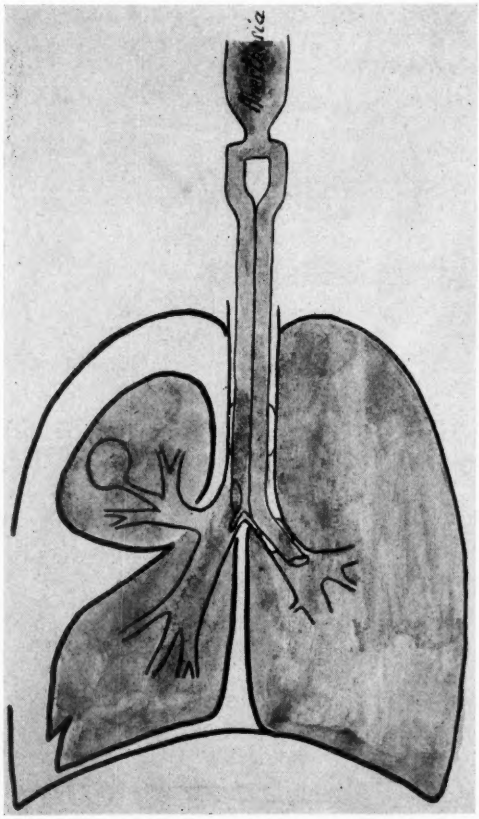

Fig. 3.—The lung can be inflated when lobar and intersegmental planes are developed.

The different steps of the invagination technique are: (1) The peripheral cartilaginous ring is exposed with a small knife and removed with a small elevator without injuring the adjacent external tissues or the thin submucosal layer (see Fig. 4*A*). This will facilitate the invagination considerably. (2) Four or five terminal interrupted sutures of No. 0000 Deknatel silk are placed. (3) A continuous number 0 catgut suture will render the bronchus airtight. (4) A number 2 silk purse-string suture is then placed around each corner (the corner constituting the border between the membranous and cartilaginous portion of the bronchial wall) (see Fig. 4*B*). (5) Each corner is then invaginated and two or three further interrupted silk sutures will complete the

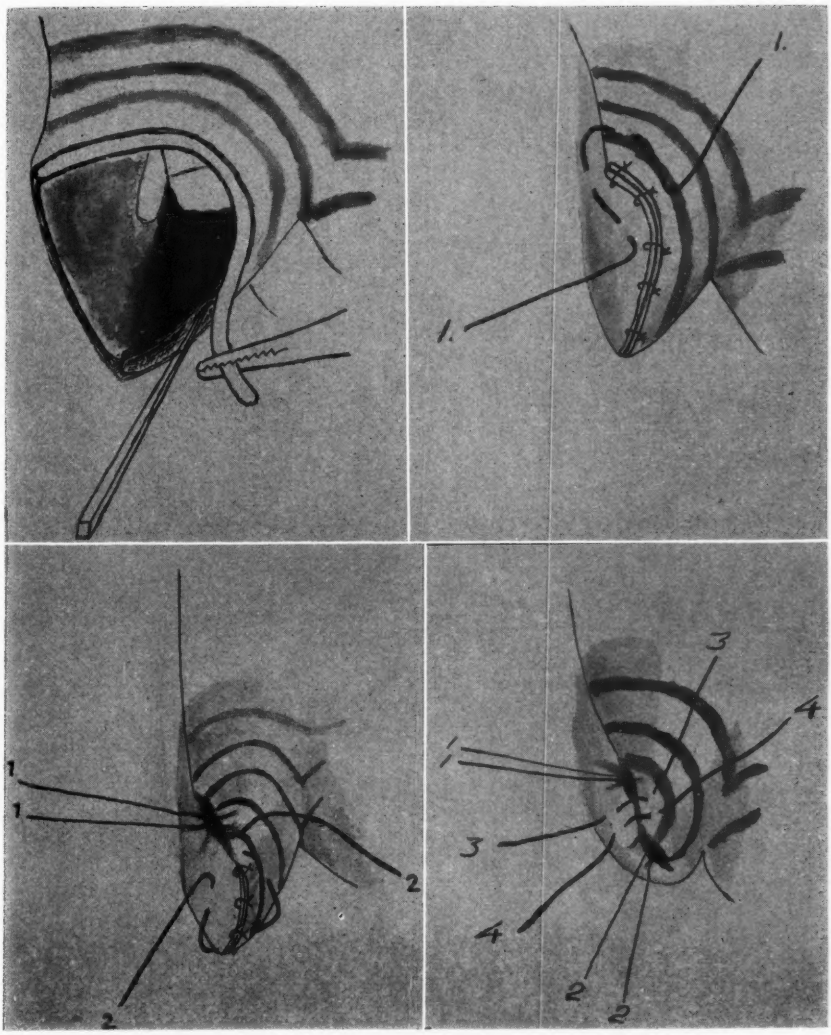

Fig. 4*A*.—The peripheral cartilaginous ring is removed by a small elevator. The rubber hook of the tube is riding over the carina.

Fig. 4*B*.—The first purse-string suture is placed (1-1).

Fig. 4*C*.—One corner has been invaginated and the second purse-string suture is placed (2-2).

Fig. 4*D*.—The invagination is completed by further interrupted silk sutures (3-3 and 4-4).

invagination. Thus several millimeters of the external bronchial wall lie pressed together facilitating healing (see Fig. 4*E*). (6) Then a pedicled pleural flap is sewn over the bronchus.

II. Simple Bronchial Closure.—In neoplastic disease the most radical resection must be carried out. Thus the bronchus is often too short for invagination. With the aid of the double-lumen catheter the resection of the right lung, cutting out the bronchus from the trachea including carina and a portion of the left main bronchus can be performed at ease. This is illustrated in Case 1, Fig. 5.

Fig. 4*E*.—Diagram of the invagination showing several millimeters of the external bronchial wall lie pressed together.

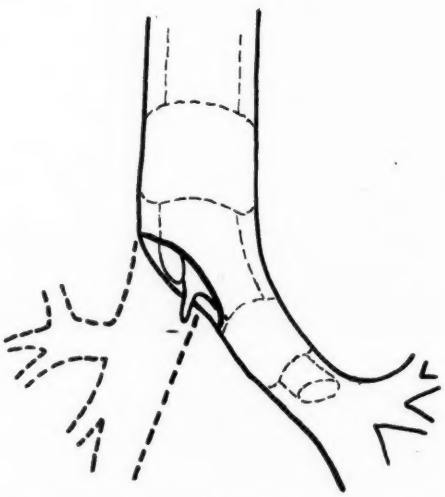

Fig. 5.—(Case 1.) High resection of right sided carcinoma including carina, part of trachea and the left main bronchus.

Fig. 6*A*.—(Case 2.) Bronchogram of the adenoma projecting into the trachea, obstructing the right and most of the left main bronchus. The abnormal right upper-lobe bronchus is seen originating from the trachea.

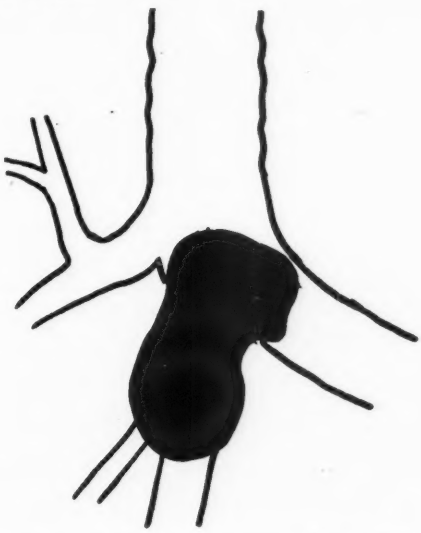

Fig. 6*B*.—Diagram of the adenoma in Case 2.

CASE 1.—A 50-year-old man was found to have a squamous-cell carcinoma of the right upper lobe, diagnosed at bronchoscopy. At operation a frozen section of the main bronchus close to the carina showed invasion of cancer. Then a portion of trachea and the carina with adjacent part of the left main bronchus was resected. Closure was then made with interrupted and a continuous terminal suture of fine braided stainless steel. A pleural flap was sewn over the suture. The postoperative course was uneventful.

Fig. 7.—Bronchography after the preoperative endoscopic coagulation of the adenoma in Case 2.

In cases of bronchial adenoma the tumor with its extra- and intrabronchial portion can be cut out from the wall of the trachea or the bronchus and a plastic repair of the defect can be performed, see Cases 2 and 3.

CASE 2.—A 39-year-old woman was found to have a bronchial adenoma obstructing the right main bronchus and most of the left main bronchus. The patient was then breathing only with the right upper lobe through an abnormal bronchus originating in the trachea 2 cm. above the carina (see Fig. 6).

After thirteen endoscopic electrocoagulations both lungs were areated. Bronchography showed the origin of the tumor in the right main bronchus and bronchiectasis in the right middle and lower lobe (see Fig. 7).

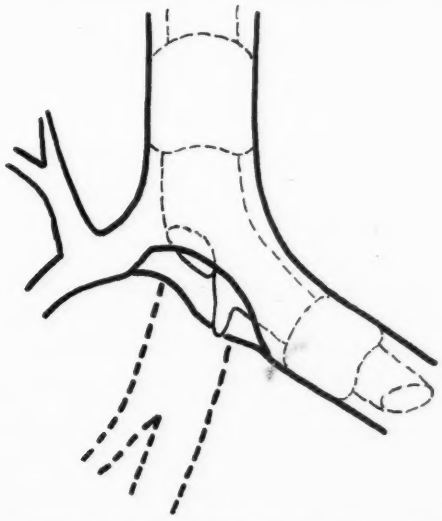

Fig. 8.—Diagram of the resection of the right lower and middle lobes including the carina and a small area of the left main bronchus in Case 2.

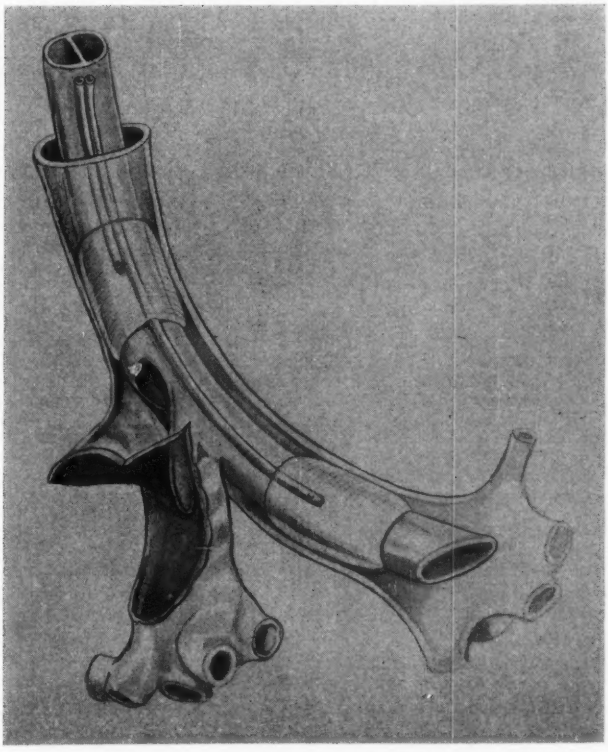

Fig. 9.—The right upper-lobe bronchus has been excised from the trachea.

At the operation the right lower and middle lobes were removed together with the carina and a small area of the left main bronchus (see Fig. 8). Closure was made by five interrupted and a continuous suture of fine braided stainless steel. The postoperative course was uneventful.

CASE 3.—A 44-year-old woman had a bronchial adenoma causing atelectasis of the right upper lobe. The right upper-lobe bronchus took its origin from the trachea at the level of the carina. At operation, the right upper lobe was removed, its bronchus being excised from the tracheal wall (see Fig. 9).

The technique of the simple bronchial closure is: (1) Dissection and removal of the peripheral bronchial cartilaginous ring. Cartilage has a poor blood supply and does not take part in healing. Sutures of braided stainless sutures of 0000 Deknatel silk on an atraumatic needle are placed. (3) Then a continuous suture of terminal 0000 Deknatel silk on a curved atraumatic needle is made. (4) A pedicled pleural flap is sewn over the bronchus.

Lobectomies and segmental resections may be performed in the same manner on the right as on the left side, but in cases of left pneumonectomies the described open closure of the bronchus cannot be carried out. When the lung is liberated and the hilar structures dissected, the cuffs are deflated and the catheter is withdrawn about 5 centimeters. Immediately beforehand the bronchial secretion on the left side is aspirated to prevent spread. Afterwards the proximal cuff only is reinflated, both lumina connected with the anesthesia machine and the catheter is used as a single lumen intratracheal tube. In the same moment as the catheter is withdrawn, a soft aortic clamp is placed at the origin of the bronchus.

SUMMARY

One lung anesthesia makes it possible to cut through the bronchus whenever this is suitable during the resection and to leave it open until it is convenient to close it. It is not necessary to apply a clamp on the proximal part of the bronchus. Resection of the carina with adjacent part of trachea and left main bronchus is greatly facilitated.

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THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

Thirty-Second Annual Meeting

May 8, 9, and 10, 1952, Baker Hotel

Dallas, Texas

Program

Thursday Morning, May 8, 1952

9:00 A.M. Business Meeting

9:30 A.M. Scientific Session

1. **Experimental Methods for Detection of Changes of Blood Supply to the Heart.**
   Alfred Goldman, Clinton Shaw (by invitation), Eliot Corday (by invitation), Joshua Fields (by invitation), S. Rexford Kennamer (by invitation), Allen Smith (by invitation), Inga Lindgren (by invitation), and Myron Prinzmetal (by invitation), Los Angeles, Calif.
2. **Artificial Oxygenation and Circulation During Complete Bypass of the Heart.**
   James A. Helmsworth, Roger T. Sherman (by invitation), Samuel Kaplan (by invitation) and Leland C. Clark (by invitation), Cincinnati, Ohio
3. **Some Physiological Aspects of the Artificial Heart Problem.**
   F. D. Dodrill, Edward Hill (by invitation) and Robert Gerisch (by invitation), Detroit, Mich.
4. **Technique of Producing Mitral Stenosis of Controlled Degree.**
   Robert G. Ellison, Robert C. Major, Raymond W. Pickering (by invitation) and Wm. F. Hamilton (by invitation), Augusta, Ga.
5. **Surgical Approach for Stenotic Lesions of the Semilunar Valves by Excision and Cusp Replacement under Direct Vision.**
   Robert S. Litwak (by invitation), and Howard L. Gadboys (by invitation), Boston, Mass.
6. **Experimental Pulmonary Venous Occlusion.**
   C. Rollins Hanlon, David Sabiston (by invitation), and Donald R. Burke (by invitation), St. Louis, Mo.

Thursday Afternoon, May 8, 1952

2:00 P.M. Scientific Session

7. **Localized Fibrous Mesothelioma of the Pleura.**
   O. Theron Clagett, John R. McDonald (by invitation), and Herbert W. Schmidt (by invitation), Rochester, Minn.
8. **Resection of the Trachea for Carcinoma—Report of Two Cases.**
   Bert H. Cotton and Joao R. F. Penido (by invitation), Beverly Hills, Calif.
9. **The Surgical Treatment of Carcinoma Involving the Hypopharynx, Larynx, and Upper Esophagus.**
   Orville F. Grimes (by invitation) and H. Brodie Stephens, San Francisco, Calif.
10. **A Consideration of Palliative Treatment with Direct Attacks upon Carcinoma of the Esophagus.**
    Mark M. Ravitch, Henry T. Bahnson (by invitation) and Thomas N. P. Johns (by invitation), Baltimore, Md.

11. **A Pathologic Study of Large Tissue Sections of Bronchogenic Carcinoma.**
Edward J. McGrath and Edward A. Gall (by invitation), Cincinnati, Ohio
12. **The Use of Streptokinase-Streptodornase (Varidase) in the Management of Early Postoperative Partial Pulmonary Resections.**
C. Thomas Read (by invitation), Phoenix, Ariz.

Friday Morning, May 9, 1952

9:00 A.M. SCIENTIFIC SESSION

13. **Traumatic Aneurysm of the Thoracic Aorta.**
R. K. Hollingsworth and W. Johnston (by invitation), Martinsburg, West Virginia
14. **Healing of Extensive Cardiac Wounds.**
C. G. Thomas, Jr. (by invitation), Chapel Hill, N. C. and S. E. Ziffren (by invitation), Iowa City, Iowa
15. **Traumatic Hemopericardium and Constrictive Pericarditis.**
Johann L. Ehrenhaft and Rodman E. Taber, Iowa City, Iowa.
16. **Rupture of the Esophagus.**
Robert A. Anderson (by invitation), Tulsa, Oklahoma and George M. Curtis, Columbus, Ohio
17. **The Effects of Atelectasis on Pulmonary Arterial Blood Flow in Dogs.**
Richard M. Peters (by invitation) and Albert Roos (by invitation), St. Louis, Mo.
18. **Surgical Management of Pulmonary Emphysema.**
Gerald L. Crenshaw (by invitation) and Donald F. Rowles (by invitation), Oakland, Calif.

Friday Afternoon, May 9, 1952

2:00 P.M. EXECUTIVE SESSION

3:00 P.M. SCIENTIFIC SESSION

Address of the President—Frank B. Berry, New York, N. Y.

19. **The Care of Thoracic and Thoracoabdominal Wounds in the Combat Zone in Korea.**
Major Edward Ernest Rocky, M.C. (by invitation), A.P.O. San Francisco, Calif.
20. **War Wounds of the Chest: Experiences with 1,535 Korean Casualities in an Army Hospital Overseas.**
Major A. R. Valle, M.C. (by invitation), Tokyo

6:30 P.M. COCKTAIL PARTY—Baker Hotel.

Saturday Morning, May 10, 1952

9:00 A.M. SCIENTIFIC SESSION

21. **Silicotic and Tuberculosilicotic Lesions Simulating Bronchogenic Carcinoma.**
Frederick G. Kergin, Toronto, Ont.
22. **The Elective Resection of Nodular Tuberculosis.**
D. O. Shields (by invitation) and John S. Chapman (by invitation), Dallas, Texas
23. **The Complications and the Results of Treatment of Bronchopleural Fistula Following Resection for Tuberculosis.**
James D. Murphy, Barney B. Becker (by invitation) and H. V. Swindell (by invitation), Oteen, N. C.
24. **Plastic Sponge Prosthesis Following Resection in Pulmonary Tuberculosis.**
Joseph W. Gale and Anthony R. Curreri, Madison, Wis.

25. **The Role of the Inferior Esophageal Constrictor in the Production of Lower Esophageal Disease.**
Earle B. Kay, Cleveland, Ohio
26. **The Delayed Restoration of Oral Alimentation in Children with an Esophageal Defect Remaining after Closure of a Tracheo-Esophageal Fistula.**
N. Logan Leven and Richard L. Varco, St. Paul, Minn.

Saturday Afternoon, May 10, 1952

2:00 P.M. SCIENTIFIC SESSION

27. **Surgical Treatment for Congenital Aortico-Pulmonary Fistula: Experimental and Clinical Aspects.**
H. William Scott, Jr., and David C. Sabiston (by invitation), Baltimore, Md.
28. **Pulmonary Function after Bilateral Multiple Segmental Resection for Bronchiectasis.**
Richard H. Overholt, Benjamin Etsten (by invitation) and James H. Walker (by invitation), Boston, Mass.
29. **The Indications For and the Results of Commissurotomy for Mitral Stenosis.**
Robert P. Glover, Thomas J. E. O'Neill, James M. Harris (by invitation) and O. Henry Janton (by invitation), Philadelphia, Pa.
30. **The Cure of Two Aneurysms Associated with Patent Ductus with a Résumé of Seventy Cases of Patent Ductus Surgically Treated.**
Emile Holman and Frank Gerbode, San Francisco, Calif.
31. **Anatomical (Histological) Basis and Efficient Clinical Surgical Techniques for the Restoration of the Coronary Circulation.**
Charles P. Bailey, R. C. Truex (by invitation), George Geckeler (by invitation) and Nicholas Antonius (by invitation), Philadelphia, Pa.
32. **Pulmonary Valvulotomy: Description of a New Operative Approach with Comments about Diagnostic Characteristics.**
Harris B. Shumacker, Jr., Indianapolis, Ind.

PAPERS TO BE READ BY TITLE

1. **The Use of Viomycin with Excisional Surgery for Pulmonary Tuberculosis.**
H. E. Walkup (by invitation), James D. Murphy (by invitation) and Oscar Kanner (by invitation), Oteen, N. C.
2. **Proposed Clinical Staging of Bronchogenic Carcinoma.**
F. X. Byron, Los Angeles, Calif.
3. **Trans-Cervical Superior Mediastinal Biopsy.**
Ralph Friedlander and Benjamin Burbank, Brooklyn, N. Y.
4. **Thoracoplasty and Resection for Pulmonary Tuberculosis: Follow-up of 229 Patients Treated by Posterior Thoracoplasty, by Resection or by Thoracoplasty and Resection.**
F. A. Hughes, Jr., C. C. Lowry (by invitation) and J. W. Polk (by invitation), Memphis, Tenn.
5. **The Results of Thoracoplasty for Pulmonary Tuberculosis Eleven to Sixteen Years after Operation.**
Arthur H. Aufses and Maurice S. Harte (by invitation), New York, N. Y.
6. **Personal Experiences with 10 Consecutive Heart Wounds Treated Successfully by Pericardiotomy and Cardiorrhaphy.**
Emil A. Naclerio (by invitation), Aubre De L. Maynard (by invitation) and John W. V. Cordice (by invitation), New York, N. Y.
7. **Simultaneous Resection and Thoracoplasty for Tuberculosis.**
James E. Dailey, Houston, Texas

8. **Pulmonary Tuberculosis—A Comprehensive Analysis of 470 Cases of Excisional Surgery Operated upon at Sea View Hospital Between 1944 and 1951.**
   Louis R. Davidson, Hyman Alexander (by invitation), Bernard J. Kesner (by invitation) and Gerald J. Lustig (by invitation), New York, N. Y.
9. **Pulmonary Diestention as Seen in the Lordotic Roentgenogram.**
   Joseph Gordon and W. Berkeley Zinn (by invitation), Ray Brook, N. Y.
10. **Intrapulmonary Hematoma.**
    Colonel John M. Salyer (by invitation), Lt. Col. Robert C. Major, Major Hu A. Blake (by invitation) and Col. James H. Forsee, Denver, Colo.
11. **Chest Wall Pain.**
    E. K. Johnson and J. L. Mangiardi (by invitation), Brooklyn, N. Y.
12. **The Use of Suture Constriction of the Upper Lobe in the Treatment of Pulmonary Tuberculosis (Paulino Procedure).**
    Paul T. DeCamp, John W. Overstreet (by invitation), Thomas G. Baffes (by invitation) and Alton Ochsner, New Orleans, La.
13. **The Diagnosis of Functionally Severe Patent Ductus Arteriosus in Infancy and Early Childhood.**
    F. Mason Sones, Jr. (by invitation) and Donald B. Effler, Cleveland, Ohio.
14. **Major Thoracic Surgery in Patients over Seventy.**
    William L. Watson, William G. Cahan (by invitation) and Dorothy P. Reaves (by invitation), New York, N. Y.
15. **Value of Scalene Node Biopsy.**
    Lawrence M. Shefts, San Antonio, Texas
16. **The Present Status of Bronchography with Absorbable Water-Soluble Media.**
    Mordant E. Pack (by invitation), A. J. Neerken (by invitation) and Emanuel Salzman (by invitation), Denver, Colo.